Pediatric Gastroenterology Hepatology & Nutrition

M.D. and Ph.D. Fellowship Training

2012

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- Texas Medical Center Digestive Disease Center
- Department of Pediatrics
- Fellow’s Day
- Children’s Nutrition Research Center
- Texas Children’s Hospital
- Gastrointestinal Procedures Suite
- Ben Taub General Hospital
- Motility Center
- Camp SIA
- Camp K’anna
- Gastroenterology Nursing Staff
- Inflammatory Bowel Disease Center
- Peds-Cori Research Center
- Liver Center
- Center for Childhood Obesity
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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. Mark A. Gilger, 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., with nearly 800 Faculty members. It is currently 1st in National Institute of Health research funding in the national rankings of Pediatric Departments. 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 most recent 2011 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 24 clinical Faculty who perform over 17,000 outpatient and over 4,000 in-patient consultations annually (see pp. 4, 15).

Clinical training is enhanced through several Texas Children’s Hospital Centers and Clinics:
- Center for Childhood Obesity ................................................. Sarah E. Barlow, M.D., M.P.H., Director
- Gastrointestinal Procedure Suite ........................................... Douglas S. Fishman, M.D., Director
- Inflammatory Bowel Disease Center ...................................... George D. Ferry, M.D., Director
- Liver Center ........................................................................... Beth Carter, MD, Clinical Director
- Neurogastroenterology and Motility Center ......................... Bruno Chumpitazi, M.D., M.P.H., Director
- PEDS-CORI Research Center ................................................. Mark A. Gilger, M.D., Director

Research Training is enhanced by:
- NIH Institutional Training Grant (T32 DK07664) ............... Robert J. Shulman, M.D., Director
- .............................................. Robert J. Shulman, M.D., Director
- .............................................. Douglas G. Burrin, Ph.D., Associate Director

Sub Specialty Clinics:
- Aerodigestive Disorders Clinic ................................. Eric Chiou MD, Director
- Eosinophilic Disorders Clinic ..................................... Anthony Olive, M.D.
- Grow Clinic ................................................................. Carol Redel, M.D., Director
- Intestinal Rehabilitation Clinic ................................. Beth Carter, 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
- ................................................................. Robert J. Shulman, M.D., Director
- ................................................................. Robert J. Shulman, 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 - 59).

OVERVIEW OF TRAINING

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 (published in Journal of Pediatrics Gastroenterology and Nutrition 29:51,1999) 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 (p. 60-64).

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. An extended research option is offered as well. 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 and provides the trainee with the state-of-the-art knowledge and skills required for an academic career. We recommend an additional 12 months of research training for Fellows seeking an academic career with a greater emphasis on research (either basic or clinical). A substantial salary supplementation is available for eligible trainees during the fourth year, as well as Baylor College of Medicine Faculty appointment at the Assistant Professor level (p. 6).

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. 8).
## CLINICAL AND RESEARCH FACULTY

### Clinical and Research Faculty

**Pediatric Gastroenterology, Hepatology and Nutrition**

- Stephanie H. Abrams, M.D., M.S.
- Sarah E. Barlow, M.D., M.P.H.
- Douglas G. Burrin, Ph.D.
- Beth A. Carter, M.D.
- Natalie E. Carter, R.N., M.S.N., P.N.P.
- Eric Chiou, M.D.
- Bruno P. Chumpitazi, M.D., M.P.H.
- George D. Ferry, M.D., F.A.A.P.
- 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.
- Mark A. Gilger, M.D.
- G.S. Gopalakrishna, M.D.
- C.Michelle Grooms, R.N., M.S.N., P.N.P.
- Paula M. Hertel, M.D.
- Ryan Himes, M.D.
- Anne M. Hutson, Ph.D.
- Craig L. Jensen, M.D.
- Kristi King, R.D., M.S.
- Lina B. Karam, M.D.
- Richard E. Kellermayer, M.D., Ph.D.
- Kristi D. King, R.D., M.S.
- Seiji Kitagawa, M.D.
- Daniel H. Leung, M.D.
- Jennifer Maupin, R.N., M.S.N., P.N.P.
- Carmen Mikhail, Ph.D.
- Kathleen J. Motil, M.D., Ph.D.
- Anthony P. Olivé, M.D.
- Antone R. Opekun, P.A.
- Sarah M. Phillips, R.D., M.S.
- Carol A. Redel, M.D.
- Barbara S. Reid, M.D.
- Ann O. Scheimann, M.D., MSR
- Vernisha Y. Shepard, M.Ed., LPC
- Robert J. Shulman, M.D.
- Kalpesh H. Thakkar, M.D., MSCR
- Sundararajah Thevananther, Ph.D.
- Bryan S. Vartabedian, M.D.

### Associated Clinical Faculty

- Bincy Abraham ............................................................... Adult Gastroenterology
- Mary L. Brandt ............................................................... Pediatric Surgery
- Darrell L. Cass, M.D .......................................................... Pediatric Surgery
- Danita Czyzewski, Ph.D ..................................................... Psychiatry & Behavioral Sciences
- Milton J. Finegold, M.D ..................................................... Pathology
- John A. Goss, M.D ............................................................. Transplant Surgery
- Nancy M. Hurst, Ph.D ......................................................... Neonatology
- Paul K. Minifee, M.D .......................................................... Pediatric Surgery
- Jed G. Nuchtern, M.D .......................................................... Pediatric Surgery
- Oluyinka Olutoye, M.D., Ph.D ............................................. Pediatric Surgery
- Christine O’Mahony, M.D ..................................................... Transplant Surgery
- David E. Wesson, M.D .......................................................... Pediatric Surgery

### Associated Research Faculty

- Arthur L. Beaudet, M.D ..................................................... Pediatrics, Molecular and Human Genetics
- Karl-Dimiter Bissig, M.D., Ph.D ........................................... Molecular and Cellular Biology
- Lawrence C. Chan, M.D ..................................................... Medicine, Molecular and Cellular Biology
- Margaret E. Conner, Ph.D ................................................... Molecular Virology and Microbiology
- Elizabeth J. Dial, Ph.D ....................................................... Integrative Biology and Pharmacology, University of Texas, Houston
- Hashem B. El-Serag, M.D ..................................................... Medicine, Gastroenterology and Health Services
- Mary K. Estes, Ph.D ............................................................. Medicine, Molecular Virology & Microbiology
- Milton J. Finegold, M.D ....................................................... Pediatrics, Pathology
- David Y. Graham, M.D ....................................................... Medicine, Gastroenterology, Molecular Virology and Microbiology
- Farook Jahoor, Ph.D ............................................................ Pediatrics, Children’s Nutrition Research Center
- Brendan Lee, M.D., Ph.D ...................................................... Pediatrics, Molecular and Human Genetics
- Lenard M. Lichtenberger, Ph.D .............................................. Integrative Biology and Pharmacology, University of Texas, Houston
- Lopa Mishra, M.D ............................................................... Medicine, Gastroenterology, University of Texas, Houston
- David D. Moore, Ph.D .......................................................... Molecular and Cellular Biology
- Betty L. Slagle, Ph.D ........................................................... Molecular Virology and Microbiology
- C. Wayne Smith, M.D .......................................................... Pediatrics, Leukocyte Biology
- James Versalovic, M.D., Ph.D .............................................. Pathology & Immunology, Genetics, Molecular Virology and Microbiology
- Robert A. Waterland, Ph.D ................................................... Pediatrics, Children’s Nutrition Research Center
- William W. Wong, Ph.D ....................................................... Pediatrics, Children’s Nutrition Research Center
- Huda Y. Zoghbi, M.D ........................................................... Pediatrics, Molecular and Human Genetics
M.D. RESEARCH TRAINING / COURSEWORK

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 month during the first year is optional. The preferred allocation is:

<table>
<thead>
<tr>
<th>Clinical Training (months)</th>
<th>Research Training (months)</th>
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</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>8</td>
</tr>
<tr>
<td>Year 2</td>
<td>0</td>
</tr>
<tr>
<td>Year 3</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
<tr>
<td>Junior Faculty*</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
</tbody>
</table>

* Offered as part of the NIH T32 Training Grant (see p. 8).

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. The Gastroenterology portion of the course is based on the text, *Pediatric Gastrointestinal Disease*, edited by Walker, Goulet, Kleinman, Sherman, Shneider and Sanderson. The Hepatology portion is based on the text, *Liver Diseases in Children*, by Suchy, Sokol and Balistreri. The Nutrition portion is based on the *Pediatric Nutrition Handbook*, published by the Committee on Nutrition of the American Academy of Pediatrics. A copy of each textbook is given to each trainee. 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.

- **Fundamentals of Clinical Investigation:** A course is offered each July/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. An optional computer literacy course is offered in conjunction with this course.

Optional Coursework:
Molecular biology impacts all aspects of modern medicine and it is imperative that Fellows be conversant with the basic tenets of this discipline. Thus, Fellows are encouraged to update their knowledge, if necessary, by taking the eight lecture unit entitled, “Introduction to Molecular Biology,” which is offered each September as part of Baylor College of Medicine core curriculum for medical students.

To enhance future research opportunities, Fellows are strongly encouraged to take the Baylor College of Medicine course entitled, “Grants and Contracts”. This course typically consists of nine weekly one-hour sessions during January and February. It is an outstanding introduction to the scientific, strategic and administrative aspects of grantsmanship.
Dr. Carol Redel is the Director of Clinical Training. The other members of the clinical Faculty are listed on page 4.

Inpatient: All Fellows receive 12 months of inpatient training in clinical Gastroenterology, Hepatology and Nutrition at Texas Children's Hospital. The inpatient service is divided into three “teams,” of which typically two teams consist of a Fellow and an attending physician. The teams alternate call days with the on-call team being responsible for consults. The third team may or may not have a fellow assigned; this team handles daytime consults at Texas Children's Hospital and affiliated institutions. The fellow assigned to the third service will not be responsible for outside consults.

- Consults are done on an average of four to six new patients each day. In addition to consults, patients cared for by the Fellow also may be admitted directly to the team, 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 physician. 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” twice a week on alternating days: Weekend call usually occurs every nine weeks for each Fellow. Fellows take night call and weekend call from home.
- 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.

- The Fellow has responsibility for continuity patients through a weekly 1/2 day Fellows’ Clinic. Staffed by selected teaching faculty, during Fellows’ Clinic there is exposure to initial evaluation and diagnostics, clinical management, and follow up for the duration of 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 Liver Center Clinic and the Inflammatory Bowel Disease Clinic. Patient continuity is provided through four-month block assignments to each clinic.
- Optional outpatient rotations include the General Gastroenterology Clinics, Eating Disorders Clinic, Feeding Disorders Clinic, Prader-Willi Clinic, Grow Clinic, and Intestinal Rehabilitation Clinic.

Skills: Expertise that the trainee will acquire includes:

- Diagnostic and management skills in a wide array of gastrointestinal, hepatic 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), liver biopsy, 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:

- The Liver Transplant Program is fully integrated into the care of pre/post liver transplant patients within the Liver Center. In order to provide optimal care for these complex patients, a “team approach” is practiced using our surgeons, transplant surgeons, coordinators, hepatologists, and other care givers.
- The Grow Clinic provides multidisciplinary evaluation and treatment of children with psychological and/or physiological feeding problems. The Grow Clinic evaluates and treats infants and children with failure to thrive or failure to eat.
- The Prader-Willi Clinic provides comprehensive treatment of this genetic disorder.
- The Inflammatory Bowel Disease Clinic provides consultation for the complex medical and psychosocial aspects of this disorder.
- The Motility Clinic provides evaluation, therapy, and research of childhood functional and motility gastrointestinal disorders.
- The Intestinal Rehabilitation Clinic is dedicated to comprehensive care of infants and children with pediatric intestinal failure.
- The Rett Syndrome Clinic provides evaluation and management of children with Rett Syndrome, which is characterized by mental retardation, autism, stereotypic hand movement and growth failure.
- The Hepatitis Clinic provides evaluation and treatment to children with viral hepatitis.
- The Aerodigestive Clinic in collaboration with the Sections of Otolaryngology and Pulmonary provides comprehensive evaluation and care of children with aerodigestive disorders.
M.D. RESEARCH TRAINING / BASIC SCIENCE VS. CLINICAL

CHOICE OF BASIC SCIENCE OR CLINICAL RESEARCH PROJECT

M.D. Fellows may choose either a basic science or clinical research project. Because few Fellows have had basic science training, it is expected that one or more of their research rotations in the 1st year will be in a basic science laboratory (see overview p. 8). Our experience is that many Fellows decide to pursue basic science after their research rotations. Ultimately, it is the Fellow's choice whether to pursue a basic science or clinical project.

BASIC SCIENCE PROJECT

All basic science mentors have extensive experience working with M.D. Fellows. Even Fellows who have had no exposure to basic science, after a short time, find themselves comfortable in this environment because of the mentor's ability to successfully integrate M.D. Fellows into their laboratory. As noted on page 5, Fellows also are encouraged to take the eight lecture unit entitled, "Introduction to Molecular Biology," which is offered each September as part of Baylor College of Medicine core curriculum for medical students to expedite their education if needed.

CLINICAL RESEARCH PROJECT

Fellows choosing a clinical project will work with their mentor to develop a protocol for approval by the Baylor College of Medicine Institutional Review Board. Because the size of our patient population is unsurpassed, opportunities for clinical research abound.

As part of this program, Fellows who choose a clinical research project and are approved for support by our NIH T32 Training Grant enter the Clinical Scientist Training Program (CSTP) at Baylor College of Medicine in their 2nd year of Fellowship (1st year on the NIH T32 Training Grant). The CSTP offers an M.S. degree in clinical investigation through the BCM Graduate School of Biomedical Sciences. Three core courses in the CSTP are: a) Fundamentals of Clinical Investigation - modules include Interpreting the Clinical Research Literature, Ethics in Clinical Research, Clinical Trial Design and Analysis, Biostatistics; b) Clinical Investigation for the Career Scientist - modules include Grant Writing, Translational Research, Leadership training, Health Services Research, and Clinical Decision Analysis; and c) Seminar - where Fellows present their research to the class, starting with the hypotheses and specific aims, and advancing to the methods and analyses. They receive constructive criticism from the course directors as well as their peers. During this period Fellows write a K23 research grant proposal.

APPOINTMENT AS JUNIOR FACULTY

M.D. Fellows who are appointed to the NIH T32 Training Grant (see p. 8) have the potential to extend their research training an additional 12 months. Fellows that choose this option receive a Faculty appointment at the Assistant Professor level in addition to a substantial salary increase offered by the Department of Pediatrics. This offer is extended to Fellows who submit an application for external research funding prior to the start of the fourth year of training. This unique opportunity not only provides financial stability, but also the ability to significantly advance the Fellow’s academic career.
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.

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 an individual research committee including the mentor and three (or more) additional members. Dr. Burrin serves as chairman of the research committee.

Using research committee 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 committee at least once 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 in academic medicine. M.D. Fellows apply for Training Grant support in the Spring of their first year of Fellowship. The Training Grant provides research support for up to 36 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. Further, 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

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 visit Baylor College of Medicine, 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 and 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 cutting edge 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.
CONFERENCES / VISITING FACULTY / BENEFITS

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>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>12:00 - 1:00 p.m.</td>
<td>* † GI Research Workshop (first and third Monday)</td>
</tr>
<tr>
<td></td>
<td>12:00 - 1:00 p.m.</td>
<td>*GI Pathology Conference (fourth Monday)</td>
</tr>
<tr>
<td></td>
<td>12:00 - 1:00 p.m.</td>
<td>*Liver Pathology Conference (second Monday)</td>
</tr>
<tr>
<td>Tuesday</td>
<td>1:00 - 2:00 p.m.</td>
<td>GI Show &amp; Tell Conference (weekly)</td>
</tr>
<tr>
<td></td>
<td>6:00 p.m.</td>
<td>* † Journal Club#</td>
</tr>
<tr>
<td>Wednesday</td>
<td>9:30 -10:30 a.m.</td>
<td>Eating Disorders Team Conference (weekly)</td>
</tr>
<tr>
<td></td>
<td>1:00 - 2:00 p.m.</td>
<td>Liver Transplant Conference (weekly)</td>
</tr>
<tr>
<td>Thursday</td>
<td>8:30 - 9:30 a.m.</td>
<td>Children’s Nutrition Research Center Conference (weekly)</td>
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<tr>
<td></td>
<td>12:00 noon</td>
<td>IBD Conference (first and third Thursday)</td>
</tr>
<tr>
<td></td>
<td>12:00 noon</td>
<td>Clinical Research Conference (second Thursday when noted)</td>
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<tr>
<td></td>
<td>4:00 - 5:00 p.m.</td>
<td>Digestive Disease Center Research Forum (weekly)</td>
</tr>
<tr>
<td>Friday</td>
<td>8:30 - 9:30 a.m.</td>
<td>Pediatric Grand Rounds (weekly)</td>
</tr>
<tr>
<td></td>
<td>12:00 - 1:00 p.m.</td>
<td>*Pediatric Gastroenterology, Hepatology and Nutrition Course (weekly)</td>
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</tbody>
</table>

# Journal Club is held in the homes of Faculty and includes dinner. This offers an informal setting in which trainees can get to know both clinical and research Faculty associated with the program.

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

Baylor College of Medicine has a very generous vacation policy for Fellows, allowing 21 calendar days per year for vacation as well as 3 days per year leave for personal or family problems. Paid sick leave accrues at the rate of 14 calendar days per year and can be carried forward if unused. Fellows also receive a health benefits package as well as subsidized on-campus parking.
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 Nutrition, 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 of Training</th>
<th>Current Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guerrero, Roberto</td>
<td>1995-1998</td>
<td>Private Practice, Miami, FL</td>
</tr>
<tr>
<td>Hwang, Sandy</td>
<td>1995-1998</td>
<td>Private Practice, Denver, CO</td>
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<tr>
<td>Arumugam, Ramalingam</td>
<td>1996-1999</td>
<td>Clinical Assistant Professor, University of Minnesota, Minneapolis, MN</td>
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<tr>
<td>Villa, Xavier</td>
<td>1996-1999</td>
<td>Private Practice, Houston, TX</td>
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<tr>
<td>Kim, Sandy</td>
<td>1997-2000</td>
<td>Assistant Professor of Pediatrics, University of North Carolina, Chapel Hill, NC</td>
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<tr>
<td>Srisirirojanakorn, Niti</td>
<td>1997-2000</td>
<td>Raising Family</td>
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<tr>
<td>Ramirez, Alejandro</td>
<td>1998-2001</td>
<td>Assistant Professor of Pediatrics, University Missouri Medical Center, Columbia, MO</td>
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<td>Karsakul, Wikrom</td>
<td>1998-2001</td>
<td>Assistant Professor of Pediatrics, John Hopkins Hospital, Baltimore MD</td>
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<td>Wilsey, Michael</td>
<td>1999-2002</td>
<td>Clinical Assistant Professor of Pediatrics, University of Southern Florida</td>
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<td>Miqdady, Mohamad</td>
<td>1999-2002</td>
<td>Assistant Professor of Pediatrics, King Abdullah University Medical School, Amman, Jordan</td>
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<td>Carter, Beth</td>
<td>2000-2003</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<td>Patel, Dinesh</td>
<td>2000-2003</td>
<td>Private Practice, Atlanta, GA</td>
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<td>Williams, Kent</td>
<td>2001-2004</td>
<td>Assistant Professor of Pediatrics, Nationwide Children's Hospital, Columbus, OH</td>
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<td>Kurbegov, Amethyst</td>
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<td>Assistant Professor of Pediatrics, Colorado, Colorado Spring, CO</td>
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<td>Stephens, John</td>
<td>2002-2005</td>
<td>Private Practice, Ft. Lauderdale, FL</td>
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<td>Sikka, Natalie</td>
<td>2002-2005</td>
<td>Assistant Professor of Pediatrics, INOVA Medical Center, Fairfax, VA</td>
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<td>Abrams, Stephanie</td>
<td>2003-2006</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<td>Hertel, Paula</td>
<td>2003-2006</td>
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<td>Gulati, Ajay</td>
<td>2004-2007</td>
<td>Assistant Professor of Pediatrics, University of North Carolina, Chapel Hill, NC</td>
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<td>Thakkar, Kalpesh</td>
<td>2004-2007</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<tr>
<td>Zayat, Mayssa</td>
<td>2004-2007</td>
<td>Private Practice, Wichita, KS</td>
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<tr>
<td>McOmber, Mark</td>
<td>2005-2008</td>
<td>Assistant Professor of Pediatrics, University of Arizona, Scottsdale, AZ</td>
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<tr>
<td>Kim, Steven</td>
<td>2005-2008</td>
<td>Associate Staff Physician, Kaiser Permanente, Sacramento, CA</td>
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<td>Venkataraman, Priya</td>
<td>2005-2008</td>
<td>Assistant Professor, Children's National Medical Center, Washington, DC</td>
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<td>Kellermayer, Richard</td>
<td>2006-2008</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<td>Himes, Ryan</td>
<td>2006-2009</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<td>Jain, Ajay Kumar</td>
<td>2006-2009</td>
<td>Assistant Professor of Pediatrics, Saint Louis University, St. Louis, MO</td>
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<td>Hattar, Lana</td>
<td>2007-2010</td>
<td>Private Practice, Wichita, KS</td>
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<td>Mehta, Seema</td>
<td>2007-2010</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
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<td>Whitfield, Lynette</td>
<td>2007-2010</td>
<td>Assistant Professor of Pediatrics, University of Pittsburgh, Pittsburgh, PA</td>
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<td>Schaible, Tiffany</td>
<td>2009-2011</td>
<td>Assistant Professor of Pediatrics, Wake Forest School of Medicine, Winston-Salem, NC</td>
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<tr>
<td>Cantu, Samson</td>
<td>2009-2011</td>
<td>Private Practice, Fort Worth, TX</td>
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<td>Name</td>
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<tr>
<td>Hardy, Michelle</td>
<td>1994-1996</td>
<td>Associate Professor, Montana State University</td>
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<tr>
<td>Dong, Yanjie</td>
<td>1995-1996</td>
<td>Real Estate Agent, Cupertino, California</td>
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<tr>
<td>Chang, Benny</td>
<td>1996-1997</td>
<td>Assistant Professor, Baylor College of Medicine</td>
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<tr>
<td>Markesich, Diane</td>
<td>1998-1999</td>
<td>Medical Writer &amp; Editor, John M. Eisenberg Center for Clinical Decisions &amp;</td>
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<tr>
<td></td>
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<td>Communication Science</td>
</tr>
<tr>
<td>Blutt, Sarah</td>
<td>1999-2001</td>
<td>Assistant Professor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Cheng, Elly</td>
<td>1999-2001</td>
<td>Housewife and mother</td>
</tr>
<tr>
<td>Robker, Rebecca</td>
<td>2000-2002</td>
<td>Research Associate, The University of Adelaide</td>
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<tr>
<td>Madden, Charles</td>
<td>2000-2001</td>
<td>Assistant Professor, George Mason University</td>
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<tr>
<td>Dekaney,</td>
<td>2001-2004</td>
<td>Assistant Professor of Pediatrics - University of North Carolina</td>
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<tr>
<td>Christopher</td>
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<td>Shroyer, Noah</td>
<td>2002-2003</td>
<td>Assistant Professor of Pediatrics, Cincinnati Children’s Hospital Medical Center</td>
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<tr>
<td>Bressler, Jan</td>
<td>2003-2005</td>
<td>Assistant Professor of Pediatrics, University of Texas</td>
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<tr>
<td>Ochsner, Scott</td>
<td>2003-2005</td>
<td>Instructor, Baylor College of Medicine</td>
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<td>Hutson, Anne</td>
<td>2003-2005</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine</td>
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<tr>
<td>Zhou, Yong</td>
<td>2007-2009</td>
<td>Postdoctoral Fellow, University of Texas</td>
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<td>Antar, Alli</td>
<td>2007-2009</td>
<td>Postdoctoral Fellow, Baylor College of Medicine</td>
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<td>Hyser, Joseph</td>
<td>2008-2010</td>
<td>Instructor, Baylor College of Medicine</td>
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<td>Wooten-Kee, Ruth</td>
<td>2008-2010</td>
<td>Postdoctoral Fellow, Baylor College of Medicine</td>
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<tr>
<td>Mei, Yu</td>
<td>2010-2011</td>
<td>Research Fellow, Harvard Medical School</td>
</tr>
</tbody>
</table>
BAYLOR COLLEGE OF MEDICINE

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 22nd overall among the nation’s top medical schools for research and 28th for primary care and 6th for pediatrics in the United States. It has more than 3700 full-time, part-time, emeritus, and voluntary Faculty and conducts independent research amounting to more than $400 million annually. The College enrolls 725 medical students in a four-year program, approximately 911 Ph.D. graduate students, more than 943 residents and Fellows in postgraduate medicine and surgery, and 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

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, Seminar Series, and an elective (Intermediate Biostatistics at the UT School of Public Health). Fundamentals of Clinical Investigation is offered in July 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/cstp

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 $101 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 nearly 800 Faculty. Some of these Faculty members provide staffing for the Pediatric Services at Ben Taub General Hospital (a public hospital that provides 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.

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 14th 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 track 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 $25,000) from the Center in order to develop research projects suitable for external funding. www.bcm.edu/gastro/DDC
FELLOWS’ DAY
The Department of Pediatrics encouragement and support of research training is illustrated by their sponsorship of an annual Fellow’s Day at which trainees have the opportunity to present their research in either oral or poster format. The Day 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 largest federally funded human nutrition research center of its kind, with 65 full-time Faculty members and approximately 350 technical and support personnel. The CNRC is 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 11-story 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, a Research Greenhouse, and both small and large animal facilities. 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 7,000-sq. ft. Gastrointestinal Procedures Suite. The GI Procedures Suite is at the cutting edge of patient care and research. More than 1,600 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 in the top ten 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 has more than 20,000 admissions and more than 200,000 clinic visits annually. The 17-story 780,000-plus-square-foot Clinical Care Center houses most of Texas Children’s outpatient clinics. 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 of more than 6,000.

TCH recently opened a 48-acute care bed hospital (West Campus) located 25 miles from the Texas Medical Center. It houses a pediatric emergency center, surgical suites, advanced diagnostic imaging center. The TCH Pavilion for Women, located in the Texas Medical Center is due to open in 2012 enabling TCH to provide a full continuum of family-centered care to women, mothers and their babies, beginning before conception and continuing through all the years of a women’s life.

www.texaschildrens.org

BEN TAUB GENERAL HOSPITAL
This Harris County Hospital District facility also is located in the Texas Medical Center. Ben Taub General Hospital has garnered the respect of the world as an elite Level 1 Trauma Center, one of only two in the Harris County area. It is the site for the Armed Forces School of Medicine trauma training program. The medical staff is comprised of the Faculty and residents of the Baylor College of Medicine with the exception of the Oral Surgery Service. This 650 licensed-bed acute care facility is one of the nation’s busiest trauma centers, caring for more than 108,000 emergency patients each year. It houses a 50 bed neonatal intensive care unit. The Pediatric Gastroenterology Faculty are responsible for inpatient coverage and outpatient coverage at a suburban clinic.
THE MOTILITY CENTER
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. www.bcm.edu/pediatrics

THE HOUSTON CENTER FOR QUALITY OF CARE AND UTILIZATION STUDIES (HCQCUS)
The HCQCUS subsumes both the Michael E. DeBakey Veterans Affairs Medical Center Health Services Research and Development (HSR&D) Service, which is a Veteran’s Administration HSR&D Center of Excellence, and the Baylor College of Medicine, Department of Medicine Section of Health Services Research. The Houston HSR&D Center of Excellence is one of the nation’s 15 health services research and development centers of excellence funded by the Veteran’s Administration. HCQCUS includes four Research Programs (Clinical Epidemiology and Outcomes, Health Policy and Quality Program, Health Decision-Making and Communication Program, and Health Services Delivery and Organization Program), a Design and Analysis Program, an Operations Division, and an Education Program.

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/

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

THE INTER-DEPARTMENTAL TRANSLATIONAL BIOLOGY & MOLECULAR MEDICINE GRADUATE PROGRAM (TBMM)
The TBMM is a new complimentary approach to train Ph.D. trainees in translational biology and promote collaborations between clinical and basic science Faculty. This innovative program aims to develop a new breed of Ph.D. scientist with firsthand experience in translational research and leadership training to serve as a catalyst to move discoveries effectively between bench and bedside. TBMM is one of 23 programs around the country supported by the Howard Hughes Medical Institute Med into Grad Initiative which is designed to develop a cadre of Ph.D. researchers who have an understanding of medicine and pathobiology and are committed to working at the interface of the basic sciences and clinical medicine. This program facilitates interactions between basic science and clinical researchers. Courses in the TBMM are available to Ph.D. trainees in our Fellowship program. www.bcm.edu/tbmm
EDUCATIONAL ENVIRONMENT

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.

www.texaschildrens.org/carecenters/GINutrition/Camps.aspx

CAMP K’ANNA
Camp K’aana is an innovative, multi-disciplinary, outcome-based, skill-learning, and fun-based summer camp program geared towards the treatment of childhood obesity. This is a 2-week residential camp with 3 reunions taking place 3 months, 6 months and 12 months after camp. Weekly planning meetings occur in association with the TCH Center for Childhood Obesity meetings. In addition to assisting with the camp planning and reunions, Fellows have volunteer opportunities with outcomes data collection, providing education to children and families, planning and participating in camp reunions, and providing medical coverage during the 2-week camp.

www.texaschildrens.org/carecenters/GINutrition/CampKAnna.aspx

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.

www.texaschildrens.org/carecenters/GINutrition/Nursing

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.

www.texaschildrens.org/carecenters/GINutrition/PEDSCORI

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 pediatric surgeons and liver specialists provide first-level clinical care to children with all forms of pediatric liver disease. Within the Liver Center, the Biliary Atresia Clinic provides comprehensive medical, surgical and transplant care for infants and children with biliary atresia. Other conditions the Center treats include chronic liver disease, fatty liver disease and hepatitis A, B and C. The Liver Center performs more pediatric liver transplants than any other hospital in the South, with survival rates well above the national averages.

www.texaschildrens.org/carecenters/liver

CENTER FOR CHILDHOOD OBESITY
The Obesity Center provides medical, psychosocial, and behavior evaluation of overweight and obese children who need care for weight and obesity-related conditions. The Center makes referrals to subspecialty offices and coordinated weight control programs. Weight control programs include family-based health and wellness programs, individualized, intensive behavior-based counseling, and a protocol-driven bariatric surgery program. The Center maintains a database for outcomes and it carries out clinical research studies in obesity. Ongoing projects include a residential summer camp program, a community recreation center after school program, and an obesity prevention study in primary care offices.

www.texaschildrens.org/carecenters/Obesity

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 IBD 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. As one of the six founding members of the National Pediatric IBD Consortium, the Inflammatory Bowel Disease Center offers patients access to the latest advances in therapies through clinical trials.

www.texaschildrens.org/carecenters/GINutrition/InflammatoryBowel
THE TEXAS MEDICAL CENTER

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 93,000 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 two medical schools (Baylor College of Medicine and The University of Texas Medical School at Houston) and nine 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 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 four 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 ranked first among the Top Ten Best Cities to live, work, and play by Kiplinger’s Personal Finance Magazine. Houston ranks among the top three cities nationally in financial support of the arts. 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. 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 new, 12-acre, downtown park featuring arts, entertainment, and children & family events.

Houston is also a sports city. Outdoor sports abound due to the year-round mild climate, and the beaches of Galveston are only an hour away. For spectator sports fans there are the former NBA World Champion Houston Rockets in the new Toyota Center and the three time reigning WNBA World Champion Houston Comets basketball teams. The Houston Astros baseball team, 2005 National League Champs, is located in a new downtown stadium, Minute Maid Park. Professional football returned to Houston in 2002 with the Houston Texans in Reliant Stadium. The Houston Dynamo, the champions of major league soccer in 2006 and 2007 will have a new stadium near downtown. Houstonians now have a new way to travel to downtown for the arts and sporting events with the expanding METRO light rail.
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<tr>
<th>Faculty Name</th>
<th>Research Interests</th>
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<tr>
<td>Abrams, Stephanie H.</td>
<td>Nonalcoholic Fatty Liver Disease &amp; Childhood Obesity</td>
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<td>Barlow, Sarah E.</td>
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<tr>
<td>Beaudet, Arthur*</td>
<td>Prader-Willi Syndrome and Obesity; Hepatocyte Gene Therapy</td>
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<td>Bissig, Karl-Dimiter</td>
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<td>Burris, Douglas G.</td>
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<td>Carter, Beth A.</td>
<td>TPN (Total Parenteral Nutrition) – Associated Cholestasis</td>
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<tr>
<td>Chan, Lawrence C.</td>
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<td>Chiou, Eric</td>
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<td>Chumpitazi, Bruno P.</td>
<td>Clinical Diagnosis, Treatment, &amp; Outcomes of Pediatric Functional and Motility GI Disorders</td>
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<td>Conner, Margaret E.</td>
<td>Pathogenesis of Intestinal Viral Infections</td>
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<tr>
<td>Dial, Elizabeth J.</td>
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<tr>
<td>El-Serag, Hashem B.</td>
<td>Clinical Epidemiology and Outcomes of GI and Liver Disorders</td>
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<tr>
<td>Estes, Mary K.</td>
<td>Gastrointestinal Virus-Cell Interactions, Pathogenesis and Immunity</td>
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<td>Ferry, George D.</td>
<td>Pediatric Inflammatory Bowel Disease Research</td>
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<td>Finegold, Milton</td>
<td>Cholestatic and Neoplastic Liver Diseases in Children</td>
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<td>Fishman, Douglas</td>
<td>Advances in Therapeutic Endoscopy (with an emphasis on pancreaticobiliary disease)</td>
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<td>Gilger, Mark A.</td>
<td>Infections of the GI Tract/Endoscopy in Children: Techniques and Outcomes</td>
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<td>Hertel, Paula M.</td>
<td>Biliary Atresia and the Neonatal Response to Rotavirus Infection</td>
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<td>Hutson, Anne M.</td>
<td>MicroRNA Regulation in the Intestine</td>
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<td>Jahoor, Farook</td>
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<td>Kellermayer, Richard</td>
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<td>Lee, Brendan</td>
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<td>Leung, Daniel</td>
<td>Pediatric Viral Hepatitis and Cystic fibrosis related liver and gastrointestinal disease</td>
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<td>Lichtenberger, Lenard M.</td>
<td>GI Mucosal Barrier Function in Health and Disease</td>
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<td>Regulation of Growth of Intestinal Polyps and Tumors</td>
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<td>Thevananther, Sundararajah</td>
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<td>Versalovic, James</td>
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<td>Waterland, Robert A.</td>
<td>Early Nutritional Influence on Mammalian Epigenetics</td>
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<td>Wong, William W.</td>
<td>Targeting Chronic Disease by Botanicals, Prevention of Childhood Obesity</td>
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<tr>
<td>Zoghbi, Huda Y.</td>
<td>Molecular Genetic Approaches to Cell Specification and Degeneration</td>
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* Bold font indicates a Training Grant Mentor
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<td><strong>Sundararajah Thevananther, Ph.D.</strong></td>
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<td>Director, Gas-Isotope-Ratio Mass Spectrometry Laboratory</td>
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<td><em>Huda Y. Zoghbi, M.D.</em></td>
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<td></td>
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<td>Investigator of Howard Hughes Medical Institute, Pediatric Neurology Division</td>
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My research focus is nonalcoholic fatty liver disease (NAFLD) in obese children. I obtained a Masters of Science in Clinical Investigation in the BCM Clinical Scientist Training Program. Currently, I have two major projects. The first is investigating the role of small bowel bacteria in the pathogenesis, severity, and treatment of non-alcoholic steatohepatitis (NASH). Investigations have included chart review of all children undergoing hydrogen breath testing for small bowel bacterial overgrowth (SBBO) in an effort to identify if SBBO is more common in overweight and obese children. Additionally, a study is underway to identify if SBBO is more common in obese children with biopsy-proven NASH versus obese children with no evidence of liver disease versus lean children without evidence of liver disease. These pilot studies will serve to provide preliminary data for an application for an NIH K23 grant looking at VSL#3, a combination of seven strains of probiotic bacteria, as a treatment for children with biopsy-proven NASH. An application for an investigational new drug (IND) with the Food & Drug Administration (FDA) is underway.

My second area of investigation includes evaluating metformin versus vitamin E versus placebo as treatments for pediatric NAFLD. This is a multi-center, NIH sponsored trial within the realm of the NASH CRN (Clinical Research Network). Baylor College of Medicine is a subcontract of St. Louis University. This is a 96-week treatment trial, which includes visits every 12 weeks with a liver biopsy performed at week 96. While ALT is the primary outcome measure, secondary outcomes including histology, dual energy X-ray absorptiometry (DEXA), activity, diet, fibrosis markers, and inflammatory markers will also be assessed. The NASH CRN was just renewed in 2011 and Baylor College of Medicine will participate.

Email: shabrams@bcm.edu
Recent Publications


The focus of my research is the care of childhood obesity, especially in the community healthcare setting. Recent studies demonstrated the ability of primary care pediatricians to recognize childhood overweight and obesity. This recognition was not associated with use of body mass index (BMI) except when BMI levels were modestly elevated. Two qualitative studies, with pediatricians and with parents of overweight and obese children, were formative in developing a pilot project aimed at increasing a parent’s desire to improve their child’s eating and physical activity routines. This project activates parents before well-child visits to seek guidance during the visit on their child’s eating or activity behaviors and facilitates semi-tailored advice from the provider.

The Obesity Center completed a pilot project demonstrating effectiveness of a community after-school program through the Houston Parks and Recreation Program. These data are published, and a larger, multi-center trial has been funded. A second research project focuses on the effect of a two-week residential summer camp program for weight loss. A pilot project demonstrated effectiveness, and a larger program is planned.

Future work will aim at linking primary care interventions with community programs.

Email: sbarlow@bcm.edu
Prader-Willi Syndrome and Obesity:
Hepatocyte Gene Therapy

Recent Publications


Our laboratory studies genomic imprinting, both the basic biology and genetics of the process, and more specifically, as it relates to Prader-Willi syndrome (PWS), Angelman syndrome (AS), and autism. Genomic imprinting is the phenomenon of differential expression of the two alleles at an autosomal locus based on their parent of origin; usually one allele is expressed and the other silenced. PWS, AS, and autism are distinct human disorders characterized by neurobehavioral abnormalities and mental retardation. PWS is caused by paternal deficiency for chromosome 15q11-q13, while AS is caused by maternal deficiency for the same region. Recent results indicate that PWS is caused by deficiency of a noncoding RNA designated snoRNA HBII-85. The function of this noncoding RNA is unknown, although indirect evidence might suggest a role in alternative splicing of mRNA. A major focus at present is to identify the function of the HBII-85 snoRNA and to understand the mechanism whereby it leads to the obesity seen in PWS. We believe that it is quite likely that identification of a clear molecular genetic mechanism for the obesity in PWS would be of relative interest to obesity as a general health problem.

The laboratory has made significant progress over the last four years in using helper-dependent adenoviral (HD-Ad) vectors to achieve gene therapy for inborn errors of metabolism that affect hepatocytes. We have conducted extensive preclinical studies in mice, dogs, and baboons and have demonstrated that this type of adenoviral vector is substantially superior to earlier generations in terms of toxicity and potential for long-term gene expression. With the use of balloons in the inferior vena cava to transiently raise hepatic venous pressure, we have achieved very high levels of gene expression with very low doses of vector and minimal toxicity. Our results with HD-Ad vectors in the Gunn rat suggest that these vectors should be very suitable for treating Crigler-Najjar syndrome. We have begun to work with the FDA to obtain an IND for a clinical trial most probably starting with Crigler-Najjar syndrome or hemophilia A or B. We will focus on disorders such as homozygous familial hypercholesterolemia, organic acidemias, and neonatal males with complete OTC deficiency.

Email:abeaudet@bcm.edu
We are interested in translational research for liver disease. We have described a new xenotransplantation model for human hepatocyte transplantation into immune deficient mice (Rag2-/-/Il2-rag -/-/fah-/- or short FRG mouse). Recent advancements led to a human liver chimerism of 95% and propagation of hepatitis B and C virus in these humanized mice. Human liver chimeric mice can be used to study hepatotropic pathogens and validate new drugs against them.

Another application of the FRG mouse and interest of the lab is regenerative medicine. Regenerative medicine has been revolutionized by the induced pluripotent stem (iPS) cell technology and a lot of effort is spent in establishing autologous cell therapies. One of the major hurdles of this seemingly straightforward approach is the lack of suitable small animal models to validate the true nature of stem cell derived hepatocytes. Our laboratory has the opportunity to validate these hepatocytes and explore cell-based therapy in our xenotransplantation model. We are developing novel genomic approaches to program stem cells into hepatocytes (differentiation) or even normal skin cells into hepatocytes (transdifferentiation). We apply knowledge from developmental biology to modern tissue engineering with the final goal to establish cell-based therapy for human liver disease.

Our approach is interdisciplinary and innovative and well characterized by the term “bench to bedside”.

Email: bissig@bcm.edu
Our laboratory works on basic and translational projects designed to establish how nutritional support, enteral versus parenteral, effects 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 show that chronic PN induces hepatic steatosis, cholestasis and insulin resistance in term and premature neonatal piglets. We are currently exploring how specific nutrients in commercial lipid emulsions alter the susceptibility to PNALD. We are exploring how nutrients affect interorgan and local cellular signaling pathways involved in hepatic lipid metabolism and bile acid homeostasis. We are also testing whether the adverse metabolic phenotype induced by PN is programmed and persists beyond the neonatal period and predisposes to adolescent fatty liver disease and type 2 diabetes.

Studies also are aimed at establishing the cellular and physiological functions of glucagon-like peptide 2 (GLP-2), an FDA-approved gut hormone currently in clinical trial for treatment of adult short-bowel syndrome. Past studies in TPN-fed piglets were first to show the trophic and vasoactive actions of GLP-2 in the neonatal gut. We identified the cellular co-localization of the GLP-2 receptor in enteroendocrine cells mediating the susceptibility to PNALD. We are exploring how nutrients affect interorgan and local cellular signaling pathways involved in hepatic lipid metabolism and bile acid homeostasis. We are also testing whether the adverse metabolic phenotype induced by PN is programmed and persists beyond the neonatal period and predisposes to adolescent fatty liver disease and type 2 diabetes.

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, laser-capture microdissection, gene microarray, and confocal microscopic imaging to identify the cellular localization of specific signals involved in the metabolism, proliferation and survival of relevant cell types, including mucosal epithelial cells and hepatocytes.

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The focus of my research is to provide an understanding of TPN (Total Parenteral Nutrition)-associated cholestasis. TPN is a form of intravenous nutrition given to patients who are unable to feed via the normal enteral route due to prematurity, intestinal surgery, or other medical condition. The administration of TPN has been life-saving, but in certain settings (e.g. the premature infant with short bowel syndrome), it has been associated with the rapid development of end-stage liver disease. Risk factors for TPN-associated "cholestasis," or slow bile flow, include prematurity, infection, bowel dysfunction, and length of TPN administration. The cause of this TPN-associated liver disease is unknown. We are focused on unraveling a molecular etiology for this disease that will, in turn, help identify anticholestatic therapeutic targets to treat this condition that is primarily seen in the pediatric population.

My laboratory research has focused on a component of the lipid fraction of TPN, stigmasterol. This compound is a phytosterol, is structurally similar to bile acids, and is an obligate component of Intralipid®. We used quantitative PCR in both mouse and human liver cell lines to show that this compound antagonizes bile-acid activation of the nuclear receptor FXR (Farnesol X Receptor). We know from FXR knockout studies performed by previous investigators, that FXR is a crucial player in maintaining hepatocyte integrity and bile flow. Specifically, FXR +/- mice fed a cholic acid diet die of hepatic necrosis and liver failure within 5 days of bile acid feeding, while FXR +/+ remain unharmed (Sinal et al, Cell, 2000). We are currently exploring and furthering our preliminary data that stigmasterol (and, more broadly all phytosterols) are FXR antagonists that induce a “chemical knockout” of hepatocyte integrity in the setting of parenteral nutrition.

In 2007, I began a new collaboration with Texas Children’s neonatologists, dietitians, and pharmacists that explores the safety and efficacy of an Omega 3 fish oil-derived intravenous lipid emulsion (Omegaven®) administration to infants with TPN-associated cholestasis. This study allows previous ideas and findings from the "bench" to be brought to the bedside." I am the Center PI for a recently submitted multicenter study of pediatric intestinal failure (Pediatric Intestinal Failure Consortium, “PIFCon”). The aim of this consortium is to retrospectively look at management trends for intestinal failure and then collaborate amongst the various centers to test various medical interventions, therapies, and outcomes.
Lipid Homeostasis and Gene / Molecular Therapy for Diabetes and Obesity

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Director of Diabetes, Endocrinology Research Center – Molecular Medicine Scholars Program
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Baylor College of Medicine

Recent Publications


My laboratory research interests are all related to the regulation of nutrient metabolism: (1) type 1 and type 2 diabetes and the metabolic syndrome, (2) lipoprotein metabolism and atherosclerosis, and (3) somatic gene therapy and other molecular therapies for the treatment of diabetes and obesity.

I am interested in the molecular pathology of hyperglycemia and diabetic complications. My colleagues and I first described the appearance of insulin-producing cells in multiple extrapancreatic tissues in diabetes. We showed that the insulin-producing cells are derived from bone marrow cells that migrate from the bone marrow to multiple tissues, including the liver and adipose tissues. They may retain their bone marrow cell characteristics or they may fuse with the local cells in various tissues and organs. His laboratory further showed that the fusion of these abnormal bone marrow-derived cells with nerve cells is an important factor in diabetic neuropathy.

I developed a novel therapy for a type 1 diabetes model in mice. This therapy showed that gene therapy-mediated delivery of a transcription factor, NeuroD (together with an islet growth factor, betacellulin), to the liver of diabetic mice leads to the development of new islets in the liver. These islets produce insulin and other islet hormones, leading to complete correction of the diabetes. The gene therapy-induced islet neogenesis strategy that "cures" type 1 diabetes in mice is significant, not only for its potential as a new treatment, but also because it is the first time a single transcription factor has been shown to lead to the biogenesis of a complete organ (endocrine pancreas) in an adult animal.

In the area of metabolic syndrome and type 2 diabetes, my laboratory is investigating the role of different fat cell-specific proteins in carbohydrate and lipid homeostasis. They produced mutant mice, including those with inactivated perilipin and adipocyte differentiation related protein (ADRP), to dissect the various biochemical pathways that regulate lipolysis and energy metabolism in vivo. In collaboration with investigators at M.D. Anderson Cancer Center, we used a fast vasculature homing peptide to deliver a pro-apoptotic gene, leading to targeted ablation of adipose tissue and reversal of obesity and diabetes in mice. The laboratory is investigating the use of this "molecular liposuction" as a possible approach to the treatment of obesity in nonhuman primates.

My laboratory has worked on the molecular genetics of lipoprotein metabolism for decades. In the last decade, we have been dissecting the role of cell cycle proteins and C-reactive protein on the cell biology and progression of atherosclerosis. More recently, we worked on the role of lipid mediators as major determinants in atherosclerosis progression. In the area of gene therapy, with investigators in Molecular and Human Genetics, our lab is a leader in the application of helper-dependent adenovirus for the treatment of genetic hyperlipidemia.

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Disorders of Esophageal Motility

Recent Publications


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.

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The Neurogastroenterology and Motility Center’s principal research interests focus on functional (e.g., irritable bowel syndrome, functional abdominal pain) and motor (e.g., esophageal achalasia) gastrointestinal disorders in children. There is often a dearth of information regarding the clinical diagnosis, treatment, and therapeutic outcomes of these disorders in children.

Projects (underway or in the planning stages) include the following:

- Pharmaceutical prokinetic interventions to address gastroesophageal reflux, pseudo-obstruction, and constipation
- High-resolution manometry and capsule technology for the diagnosis of gastrointestinal motility disorders in children
- Outcomes of children receiving *Clostridium botulinum* toxin injections for gastrointestinal motor disorders
- Topical therapies for children with non-relaxing internal anal sphincter.

Identification of factors causing visceral hyperalgesia in children with functional gastrointestinal disorders

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Pathogenesis of Intestinal Viral Infections

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Recent Publications


This laboratory has recently defined and is actively investigating several new and previously unrecognized aspects of rotavirus virulence and pathogenesis. While rotavirus was thought to be a localized infection in the intestine, we recently showed that rotavirus routinely escapes the small intestine in multiple animal models and children. We are currently examining the impact of extra-intestinal rotavirus infection on pathogenesis, disease, and immunity in animals and children, defining how rotavirus escapes the intestine, whether it causes non-diarrheal disease of the gastrointestinal tract or other organs in animal models, and further defining the epidemiology of the presence of extra-intestinal rotavirus infections in children.

The first licensed rotavirus vaccine was withdrawn from the market because of an association with intestinal intussusception. Recently, post marketing surveillance data indicate that the currently licensed RotaTeq and RotaRix vaccines also pose an increased risk of intussusception. We have developed the first animal model to study rotavirus-associated intussusception. We are seeking to understand the molecular mechanisms of how rotavirus contributes to intussusception by investigating the role of epithelial cell, enteric nervous system, and intestinal smooth muscles in intussusception using multiple modalities, including application of in vivo imaging by MRI and ultrasound. Future projects will define signaling pathways and mechanisms of interaction between the pathways that control intestinal motility to gain additional insights into the mechanisms of intestinal intussusception.

IgA is critical for protection from intestinal pathogens. The small intestine contains over 80% of the total B cells in the body that produce >40 mg/kg/day of IgA. Intestinal IgA is generated as a result of T cell independent and dependent mechanisms. Many viral infections induce T cell independent (polyclonal) B cell activation. However, the cells and molecules that provide the co-stimulatory signals to B cells to induce T cell independent activation, class switch recombination (CSR) and production of IgA are not known. Our long-term goal is to understand the critical pathways that drive T cell independent B cell activation and the contribution of this activation to antigen-specific IgA production in the intestine. To meet this goal, we utilize an intestinal pathogen, rotavirus, to define T cell independent IgA responses in the intestine. Rotavirus is an excellent model system because the primary site of rotavirus replication is the small intestinal enterocytes, it is a potent inducer of intestinal IgA, and IgA is required in protection of the intestine from rotavirus re infection. Newly initiated studies are focused on the impact of the intestinal microbiota on rotavirus infection and viral-specific IgA responses.

Our studies will provide important basic information on rotavirus pathogenesis and immunity and intussusception. Additionally, the identification of new pathways of IgA induction will provide new targets that can be exploited for development of therapeutic and vaccination strategies to protect from mucosal pathogens and inflammatory disease.

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Protection of the Gastrointestinal Mucosa by Luminal Factors

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Recent Publications


The gastrointestinal mucosa maintains a barrier to acid, bacteria and their toxins that is developmentally regulated. We have focused our research on a role for elements found within the lumen on the maintenance and enhancement of this barrier function. In particular, we are interested in factors found in breast milk and the manner in which they exert their protection. Our laboratory has shown that lipids in milk, particularly phosphatidylcholine, are uniquely able to coat the GI mucosal lining and promote acid-resistance. Another element in breast milk that we have studied is lactoferrin, a large protein with growth-promoting and protective properties. Lactoferrin has been shown to exert antibiotic actions against the gastritis-inducing pathogen, *Helicobacter pylori*, as well as protection against non-steroidal anti-inflammatory drug (NSAID)-induced GI injury. The mechanisms by which lactoferrin and phospholipids protect the GI tract are under investigation and may have applications beyond pediatric uses. For example, we are also interested in methods to protect the adult GI tract from injury due to shock states such as may occur during acute systemic endotoxemia or intestinal ischemia/reperfusion injury. It may be possible to improve GI barrier properties in both children and adults by addition of these luminal elements to enteral feeding mixtures. A final area of interest is in luminal elements that may break down the GI barrier. In that regard, we have investigated roles for bile acid duodenogastric reflux and secretion of intestinal phospholipase A2 in GI barrier disruption. By interfering with the appearance or increase in these damaging factors, there is the potential for preventing GI injury and subsequent systemic effects.

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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.

We have described the recent trends in the incidence of hepatocellular carcinoma (HCC) in the United States. In a study published in the New England Journal of Medicine (1999), we described a significant increase in the incidence, hospitalization, and mortality related to HCC, and as a shift of disease burden towards younger persons. Based on these data, we hypothesized that HCV infection acquired 2-3 decades earlier was responsible for the increase in HCC. This led to subsequent analyses of national VA databases that directly linked HCV-related HCC to the increase in HCC (2000). We conducted subsequent studies that showed similar trends in incidence and causes of HCC at referral centers. We have been interested in identifying the etiology of “idiopathic” HCC, which encompasses an alarming 25% of all HCC cases in the US. We recently completed several large epidemiologic studies that provided compelling evidence for diabetes as a risk factor for HCC. This finding is particularly significant given the rising epidemic of obesity in the United States. We are also designing a population-based case-control study to examine the role of several environmental and genetic factors in HCC. Our current interests also involve the study of use and outcomes of screening and therapy of HCC in the US (currently funded through an R01 grant) as well as genetic epidemiology of HCV and NASH related liver damage.

My other major research area focuses on the epidemiology, risk factors, and the clinical course of gastroesophageal reflux disease (GERD), and Barrett’s esophagus. Our previous studies included large epidemiological studies to examine the potential extraesophageal manifestation of GERD in adults and children, and the outcomes of fundoplication in adults as well as children. We have recently completed a cohort study to examine the progression of childhood GERD into adulthood. Our current R01 funded project involves examining the role of abdominal obesity as a risk factor for Barrett’s esophagus in a study of more than 3000 subjects with and without Barrett’s. A strong collaboration with Dr. Mark Gilger from Texas Children’s Hospital has been established to conduct a multicenter study to examine the prevalence and determinants of Barrett’s esophagus in children.

I have use of large databases to detect trends in disease occurrence and outcomes, generate new hypotheses, and answer specific research questions. These databases included cancer registries, endoscopic registries, national, as well as local administrative databases. We have used the information gained in epidemiological studies to design prospective epidemiological studies of the ethnic and racial differences of the distribution of Barrett’s esophagus, as well as translational studies using microarray technology to study the global gene expression in Barrett’s esophagus.

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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. Studies on the molecular biology of the rotaviruses seek to dissect the biologic, biochemical and structural role(s) of specific genes and their protein products in facilitating virus replication and inducing disease. Current studies are determining how the first described viral enterotoxin functions to regulate virus replication and induce diarrhea by triggering cell signaling pathways after interacting with an intestinal cell receptor. Cloning and sequencing the first norovirus 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. The molecular basis for the restricted replication of Norwalk viruses to the human GI tract is being dissected by using the first infectious cDNA of NV in mammalian cells that express histoblood group antigens, recently discovered host susceptibility factors. Finally, we are evaluating pathogenesis and how to use recombinant virus-like particle norovirus vaccines to induce a protective mucosal immune response through conducting volunteer studies. Recent identification of a correlate of protection and initial efficacy studies with promising results are stimulating norovirus vaccine development.

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The IBD Center is involved in clinical studies related to early onset IBD, both clinical trials and the clinical course of disease in childhood. Studies of the natural history of IBD in early onset disease, along with future genetic and biological markers, will help define patients who need more intensive (and possibly more toxic) therapy to prevent long term complications, such as surgery. There are approximately 500 children with IBD (both Crohn’s and ulcerative colitis) that are cared for at Texas Children's Hospital. The IBD Center provides comprehensive care that includes GI staff, nursing, social services, nutritional support, psychological evaluation and surgical expertise. Patient information is captured in a web-based database run by the EMMES Corporation in Washington, DC.

The Center is one of the founding members of the Pediatric IBD Consortium and participates regularly with Consortium research projects, funded by the NIH, private foundations and/or industry. Current Consortium studies gathering data via the EMMES database include, “Gender Differences in Growth In Pediatric Patients With Crohn’s Disease,” “Genetics of Early Onset IBD,” and the “Pediatric Inflammatory Bowel Disease Consortium Registry” data gathering via the EMMES database. Consortium members include Baylor and Texas Children’s Hospital, Mass General Hospital in Boston, Children’s Hospital of Philadelphia, Emory University in Atlanta, University of California at San Francisco and Los Angeles, Kaiser Permanente of Northern California, University of Vermont, and the University of Chicago. Clinical trials include work with anti-TNF antibodies for Crohn’s disease and oral 5-ASA and 4-ASA products for ulcerative colitis. A joint protocol with Dr. James Versalovic is looking at “Probiotic Lactobacillus-Mediated Modulation of Monocytes from Children with Crohn’s Disease.” A new protocol gathering DNA samples to look at genetic variation in early onset IBD began early in 2008.

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Cholestatic and Neoplastic Liver Diseases in Children

MILTON J. FINEGOLD

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Associate Chair, Department of Pathology
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Recent Publications


Trobaugh-Lotrario AD, Finegold MJ, Feusner JH. Rhabdoid tumors of the liver: Rare, aggressive, and poorly responsive to standard cytotoxic chemotherapy. Pediatr Blood Cancer. 2010


Dr Finegold is one of the Pathology directors of the NIDDK - sponsored Consortium on Childhood cholestatic liver disease (ChIDREN). It is devoted to collaborative translational research on etiology, pathogenesis, and treatment of Extrahepatic Billary Atresia, Alagille syndrome, Cystic fibrosis, Progressive familial intrahepatic cholestasis, Alpha 1-antitrypsin deficiency and Idiopathic Neonatal Hepatitis. Fifteen major medical institutions participate and the pathologists from each them meet 3x per year to review biopsies, explants and other specimens in order to establish diagnostic criteria and plan hypothesis-driven investigations, within the committee or as part of disease-oriented committees. His special interest is in "Idiopathic" Neonatal hepatitis.

Also, Dr Finegold has been the pathologist for the Children’s Oncology Group Liver Tumor study group since 1986, for which he reviews all stage 1 and 2 hepatoblastomas in order to determine the need for chemotherapy, and all biopsies, resections or transplants as part of on-going research on treatment strategies.

Dr Finegold is Director of the Texas Medical Center Digestive Disease Center Molecular Morphology Core Laboratory, sponsored by the NIDDK. In this capacity, he acts as consultant to over 50 members of the Center and the young investigators and Fellows in their laboratories on the appropriate methods and procedures needed for their studies, as well as managing the actual work performed by the laboratory, and helping with images, interpretations and manuscript preparation.

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Our research group focuses on the care of children with pancreaticobiliary disease and I am interested in the development of new technologies within pediatric therapeutic endoscopy. Current studies include the evaluation of current techniques in endoscopic retrograde pancreatography (ERCP) and include: management of common bile duct stones in children, intraductal endoscopy, and pancreatic stent usage. We also have protocols evaluating patients with various types of gallbladder disease as part of a continued expansion of our relationship and collaboration with surgery, radiology and internal medicine colleagues in these arenas.

A related area of study is acute, recurrent and chronic pancreatitis. Texas Children’s Hospital- Baylor College of Medicine is a member of the INSPPIRE group, which is an international, multi-center collaboration to study recurrent and chronic pancreatitis in children. Finally, we also have teamed with other children’s hospitals to study gastrointestinal bleeding, choledocholithiasis management and related disorders requiring endoscopic management. Our future goals are to establish natural history patterns, propose treatment algorithms based on prospective data, and to incorporate advances in therapeutic endoscopy when appropriate.

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Recent Publications


Infections of the Gastrointestinal Tract
Endoscopy in Children: Techniques and Outcomes

Professor
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Director of PEDS-CORI Research Center
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MARK A. GILGER

We pursue applied clinical research, bringing basic science laboratory advances to the bedside. For example, areas of past research include validation of the 13C urea breath test for detection of Helicobacter pylori infection in children, Barrett’s esophagus, pediatric GERD and therapeutic endoscopy. Our areas of current research focus include:

1. Infections of the gastrointestinal tract
2. Malabsorption
3. Gastrointestinal endoscopy.

In cooperation with the laboratories of Mary K. Estes PhD, Robert Atmar, MD and David Y. Graham, MD, we continue our pursuit for a viable vaccine for Norovirus infection. Current investigations include:

1. Phase 1-2, randomized, multi-center, double-blind, placebo-controlled, safety and efficacy study in healthy adults of intranasal norwalk virus-like particle vaccine in experimental human norwalk virus infection
2. Norwalk virus culture in human intestinal tissue

In cooperation with the laboratory of Buford Nichols, M.D. & Antone Opekun, PA-C, we are studying the diagnosis and treatment starch maldigestion. For example, we have developed a new 13C starch breath test as a diagnostic tool. Current investigations include:

1. Regulation of maltase-glucoamylase in the human.
2. Fungal glucoamylase supplements on starch digestion in glucosidase deficient children.

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The Gastrointestinal Procedures Suite (GIPS) at Texas Children’s Hospital is the national headquarters of the Pediatric Endoscopy Database System – Clinical Outcomes Research Initiative (PEDS-CORI). Established in 1999, PEDS-CORI now includes information of over 80,000 pediatric endoscopies. Current investigations include:

1. The role of endoscopy in children with inflammatory bowel disease.
2. The role of endoscopy and mucosal healing in children with IBD.

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The main focus of the investigation in our laboratory is related to infectious agents and their interaction with the gut. The two pathogens that we focus on are *Helicobacter pylori* and *Norovirus*. *H. pylori* is known to be the cause of gastritis and peptic ulcer disease, and the infection is closely related to gastric carcinoma in primary gastric lymphoma. Noroviruses are a major cause of non-bacterial gastroenteritis in humans.

The *Helicobacter* program is comprehensive, and it covers areas such as new therapies, the epidemiology and transmission of the infection, the molecular epidemiology of the infection within populations and within families, as well as evolution of potential virulence factors and their role in disease pathogenesis. We have identified several important new virulence factors including an outer membrane protein we designated as oipA and the duodenal ulcer promoting factor dupA. We are currently evaluating their roles in disease causation and where it interacts in the signal transduction pathway for IL-8 production. The program uses human subjects, patients, cell lines, and animal models.

Studies relating to Norovirus involve vaccine development.

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Biliary atresia (BA) is a progressive disease of bile ducts with onset exclusively in the neonatal period, and is the most common indication for liver transplantation in children. In the “perinatal” form of biliary atresia (approximately 80% of cases), which is our research interest, children are born apparently healthy and develop signs of bile duct obstruction within 1-2 months of birth.

The cause of BA is not known, but it has been hypothesized that an insult such as exposure to a toxin or infection during the neonatal period may be responsible. Rotavirus, a common cause of diarrheal disease in childhood, is one possible etiologic agent: rotavirus was isolated from liver tissue of infants diagnosed with BA significantly more frequently than in controls with other liver diseases (Riepenhoff-Talty et al.), and a mouse model of BA has been developed in which neonatal mice inoculated with rotavirus develop a progressive inflammatory destruction of bile ducts that histologically and clinically resembles BA in human infants.

In the mouse model, we have thus far demonstrated that live, replicating virus is necessary to cause disease, that replicating virus can be identified in the biliary epithelial cells of affected bile ducts, and that serum rotavirus antigenemia occurs in animals that develop biliary atresia. We have also demonstrated that maternal immunization using non-replicating, non-infectious rotavirus virus-like particles results in production of maternal rotavirus-specific antibody, which is transferred to offspring and can prevent development of BA in these rotavirus-infected neonatal pups. This finding is particularly relevant because the rotavirus vaccine currently in use is initially given at 2 months of age, which is beyond the age that BA begins to develop.

Currently, we are studying characteristics of neonatal mice that may contribute to their unique vulnerability to developing BA following rotavirus infection; including their immune responses, which differ from those in older mice; and their bile ducts, which retain fetal characteristics and are potentially vulnerable in very early life. It is anticipated that determination of age-related factors that make the neonatal mouse susceptible to BA will shed light on potential preventive or curative measures that may be implemented in human infants with BA in the future.

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Recent Publications


The focus of my laboratory’s research is to understand how microRNAs (miRNAs) help regulate intestinal epithelial cell growth and differentiation. The intestinal epithelium is constantly undergoing self-renewal. In the small intestine, the epithelial lining is divided into crypts, small invaginations below the lumen surface, and villi, projections into the lumen. Most epithelial cells migrate from the crypts, the site of proliferation and cell fate decisions, to the villi, where differentiated absorptive enterocytes and secretory cells function. Many factors have been identified that are important for intestinal epithelial cell self-renewal, but the details as to how they are regulated remain to be fully elucidated. miRNAs are a new class of regulatory RNAs essential for cell proliferation and differentiation in all cell types examined thus far. miRNAs repress protein expression by binding the 3'-untranslated region (3'UTR) of target mRNAs. To date, there are no reports of how miRNAs function in the intestinal epithelium.

My laboratory has identified miRNAs that could be important for small intestinal epithelial cell proliferation, cell lineage fate choices, and cell differentiation. We have detected miRNAs that are differentially expressed along the crypt-villus axis, and are functionally characterizing the ability of selected miRNAs to regulate expression of important transcription factors in intestinal epithelium. These studies will augment the field of gastrointestinal biology by providing important clues as to how dysregulation of miRNA contributes to intestinal diseases.

Furthermore, miRNA-based therapies are already viewed in the pharmaceutical and medical communities as attractive candidates for small molecule drugs. With the new progress in site-specific delivery of drugs to different regions of the intestine, long lasting miRNA mimics and inhibitors could be encapsulated and delivered to the site in the intestine where they are needed. Thus, our research can help lead to the development of miRNA-based therapies to prevent the development or progression of intestinal diseases.

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Recent Publications


The primary research interests of my lab focus on the modifications of macronutrient metabolism in conditions such as diabetes mellitus, overweight and obesity, severe protein-energy malnutrition, acute and chronic infections, sepsis, pregnancy and ageing and how these modifications impact other aspects of physiological function and aspects of host defense, in particular, the capacity to synthesize the antioxidant glutathione and the acute phase proteins. The goal is to determine how these changes in turn precipitate other pathologies, and to use the metabolic information obtained to design novel therapeutic strategies to counter these derangements. To achieve these goals current research efforts utilize stable isotope tracer methodologies and a combination of animal models and patient populations. Ongoing research centers on:

- The alterations of protein and glucose metabolism in sepsis.
- Lipid and glucose metabolism in HIV infected individuals with lipodystrophy and insulin resistance.
- Sulfur amino acid metabolism and glutathione homeostasis in the pathogenesis of Kwashiorkor.
- Aromatic amino acid metabolism in children with severe childhood undernutrition.
- Determination of how maternal obesity and undernutrition alter the metabolic/physiologic adaptations necessary for a successful pregnancy.
- Role of nitric oxide synthesis in the hypotension of sepsis.

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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 develop 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 microbiomic 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. Large scale, high throughput microarray methods are employed in this process. Similar methods are utilized by us on human colonic mucosal samples to interrogate age and disease dependent epigenomic and microbiomic changes. Our studies should provide the basis for novel diagnostic, preventative and therapeutic measures for IBD.

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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 arginosuccinic 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.

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The focus of my clinical research is in viral hepatitis and cystic fibrosis. My research is dedicated to understanding the epidemiologic risk factors, immunity, and treatment of pediatric hepatitis B while focusing on its impact on morbidity and other disease states (liver transplantation, cancer, immune suppression). Ongoing and future projects include:

1) Degree of Underreporting of hepatitis B within children
2) Hepatitis B reactivation in patients with hematologic and oncologic conditions

The Viral Hepatitis Clinic at Texas Children’s Hospital is also part of a multi-national clinical trial studying the efficacy and safety of Entecavir for the treatment of chronic hepatitis B in children. In the future, I hope we will be a designated site for many clinical trials in pediatric hepatitis C and B as novel treatment options are becoming available.

Cystic fibrosis (CF) is a disease that significantly alters the gastrointestinal tract and liver. With as many as 20% of children developing liver fibrosis by the 2nd decade of life and nearly all CF children being affected by suboptimal growth, pancreatic insufficiency, abdominal pain, and diarrhea to some degree, CF is as much a hepatobiliary and gastrointestinal disease as it is a pulmonary disease. My research interest within cystic fibrosis is the natural history and progression of liver fibrosis in this cohort. I currently serve as site co-principal investigator for the NIH sponsored CFLD study Prediction by Ultrasound of the Risk of Hepatic Cirrhosis in Cystic Fibrosis (PUSH). I am also working with the Cystic Fibrosis Foundation in longitudinally characterizing the growth and nutrition in children diagnosed with CF by newborn screen while also creating a biorepository for future studies in a multi-center study. Ongoing and future projects in the area of CF include:

1) Characterizing the evolution of the intestinal microbiome of infants with CF and its impact on nutrient/vitamin absorption and longitudinal growth.

Email: dhleung@texaschildrens.org
Regulation of Gastric Barrier Function; Gastric Homeostasis in Health & Disease

Professor
Department of Integrative Biology and Pharmacology
University of Texas Medical School at Houston

LENARD LICHTENBERGER

Recent Publications


The major focus of my lab is to study the barrier properties of the upper GI tract in health and disease, and specifically the role of phospholipids in the genesis of a surface hydrophobic barrier to acid and other luminal necrotizing factors. The two areas of research that have relevance to pediatric gastroenterology, is to study the importance of this barrier in the protection of the developing gut, and in specific diseases associated with mucosal ulceration (e.g. necrotizing enterocolitis, NSAID-induced peptic ulceration, and multiple organ failure). We are currently studying the contribution of surface phospholipids in pathogenesis of NSAID-induced GI ulceration, and intestinal injury/inflammation associated with traumatic injury, that may be an important trigger in the development of multiple-organ failure. This research may have clear relevance not only in increasing our understanding of pathogenesis of digestive diseases, but in providing new therapeutic approaches to attenuate GI injury. This is underscored by the fact that we have developed a phospholipid-associated NSAID (ibuprofen-PC) that is currently in Phase II clinical trial. Trainees in the future, as in the past, will have their own independent research project that bridges the interest of the mentor’s lab and goals of the pediatric GI training grant. The trainees will be expected to present their results before the mentor’s weekly lab meeting and annually at both the local seminar series of the pediatric GI program and at a national pediatric/GI meeting.

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Regulation of Growth of Intestinal Polyps and Tumors

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MISHRA LOPA

Recent Publications


Dr. Lopa Mishra’s clinical research training was mentored by Dame Sheila Sherlock, a pioneer in clinical liver diseases, recognized by Royal Society Fellowship. Lopa’s research training at Johns Hopkins University School of Medicine was under John Gearhart’s guidance, a leader in stem cell biology. For the past 20 years, Lopa has passionately pursued liver and gastrointestinal stem cell research. Lopa discovered a group of gut stem cells that are crucial for TGF-β signaling and modulation of human gastrointestinal cancers. She was the first to demonstrate the tumor suppressor role of the adaptor protein Beta 2 Spectrin in the TGF-β pathway, translating the results rapidly into clinical care. With others, Lopa has carried out seminal work developing TGF-β pathway markers for analysis of early gastrointestinal tumors, vital to guiding therapeutics. Importantly, she has revealed that TGF-β signaling is pivotal to gut stem cell homeostasis, its absence in the gut resulting in “cancer stem cells”, and more recently a human stem cell disorder, the Beckwith-Wiedemann Syndrome. Her linking TGF-β signaling with changes in E-cadherin and β-catenin for the first time in a human disease provides important clues to a common basis for the development of human foregut cancers. Her current research focus is on mechanistic studies to identify key signaling pathways in foregut cancers, which has led to the exploration of new therapeutics targeted at liver and gastrointestinal cancer.

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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 examining the linkage of CAR to metabolic diseases and have found that it is activated by type 1 diabetes, and also that its activation by xenobiotics has a beneficial effect in type 2 diabetes.

FXR is the primary nuclear receptor for bile acids, cholesterol metabolites that are important regulators of lipid homeostasis. FXR regulates a number of key metabolic target genes including SHP, an unusual orphan receptor that lacks a DNA binding domain. SHP represses transactivation by several other nuclear receptors and decreases expression of target genes, including the rate limiting enzyme for bile acid production. We have found that FXR null mice are insulin resistant, due at least in part to elevated levels of circulating free fatty acids. Bile acids can promote liver growth, and we have found that FXR activation is essential for normal liver regeneration. Bile acids can also act as tumor promoters, and we are studying the basis for spontaneous tumorigenesis in double knockout mice lacking both FXR and SHP, which have severe liver toxicity due to uncontrolled bile acid production. We will continue to use pharmacologic and mouse knockout approaches to explore the diverse metabolic regulatory functions of the nuclear hormone receptors.

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The primary goal of my research is to understand the role of dietary and hormonal factors in the regulation of growth and body composition in girls and women with Rett syndrome, a neurodevelopmental disorder caused by a mutation in the MECP2 gene. This endeavor is relevant because the nutrient requirements for optimal health and functional performance are unknown in individuals with this rare genetic disorder.

I currently am studying the natural history of osteopenia in girls and women with Rett syndrome. I have shown that girls with Rett syndrome have profound osteopenia that may occur at an early age, despite the absence of dietary calcium and vitamin D deficiency or hyperparathyroidism. Furthermore, a defect in intestinal calcium absorption does not account for their bone mineral deficits.

My studies use balance methods, stable isotope techniques, and/or dual energy x-ray absorptiometry to characterize the adaptive responses of body mineral metabolism to dietary, hormonal, or pharmacologic perturbations. I am currently conducting a double-blind, placebo-controlled protocol that examines the role of dietary calcium supplementation on bone mineral status. The aim of these studies is to elucidate the mechanisms that contribute to bone mineral deficits and to provide recommendations for dietary calcium intakes in girls with this neurological disability.

Future research goals will address the role of novel and classic nutrients in modulating the biobehavioral outcomes of girls and women affected with Rett syndrome.

Email: kmotil@bcm.edu
Up to 46% 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: a) Characterizing the gastrointestinal microbial contribution to symptoms; b) Investigation of the contribution of abnormalities in the sympathetic and parasympathetic nervous systems and somatic and visceral sensory systems to pain experience; c) Characterizing the role of low grade gastrointestinal inflammation in producing gastrointestinal symptoms; c) Investigating the psychological contributions to pain experience; and d) Characterizing the potential 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).

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The long-term goal of our laboratory is to define the role of the HBV X protein in virus replication and in the development of hepatocellular carcinoma (HCC). HBV encodes a single regulatory protein called HBx, and although HBx is required for virus replication, the lack of virus infection models has limited progress in understanding the functions provided by HBx. We have developed and characterized two HBV replication assays that permit analysis of the role of HBx in the context of virus replication. In both transfected HepG2 cells and in hydrodynamically-injected mice, HBx is required for maximal virus replication. Current studies are focused on understanding how the HBx protein is able to block the activation of type I interferons. Transgenic mice that express HBx in their liver represent an important model in which to investigate HBx function in vivo. We are able to extend results obtained in transfected HepG2 cells into an in vivo setting that more closely resembles the hepatocyte environment in which HBV replicates. Results can be further extended into humans using our collection of 47 sets of matched normal and liver tumor tissue. Both M.D. and Ph.D. trainees are welcome to participate in all stages of this research project.

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Recent Publications


We are currently studying the inflammatory response of adipose tissue and liver in animal models of diet-induced obesity. This work focuses on the various subsets of leukocytes that are resident or emigrate into these tissues and their contributions to local and systemic complications of obesity. Current evidence indicates that T cells and macrophages are resident in adipose tissue. They increase in response to high fat diets and change their functional characteristics, producing proinflammatory cytokines and chemokines. Adipose tissue inflammation is a very early phenomenon in high fat diet-induced weight gain, and liver inflammation and steatosis are later manifestations. Our investigations are characterizing these changes and attempting to define the mechanisms of their induction by high fat diets and their modulation by subsequent weight loss. Potential mechanisms under investigation involve Toll-like receptors (TLRs) and T cell subsets. TLRs and T cells appear to be involved in the induction of these inflammatory responses, but the specific target cells (or subsets) and ligands are unknown.

A second area of investigation involves the low-density lipoprotein receptor-related protein (LRP), a multi-functional scavenger receptor located on hepatocytes, monocytes and macrophages. The diverse biologic role of LRP includes regulation of proteolytic activity, lipid metabolism, fibrinolysis, and cellular migration. Many of these activities are disrupted and contribute to the pathophysiology of sepsis and multiple organ dysfunction syndrome. Our current studies focus on the mechanisms of LRP’s involvement in the development of systemic and local inflammation. We currently have evidence that loss of hepatic LRP will result in abnormal clearance of cytokines and proteinases, and we are testing whether this will contribute to systemic or liver inflammation. We are currently developing mice with specific deletion of leukocyte LRP to assess its contributions to systemic and local inflammation.

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My research interests include endoscopy, eosinophilic gastrointestinal disease, chronic abdominal pain, GERD, and Inflammatory Bowel Disease (IBD). I have established a strong collaboration with Dr. El-Serag and Dr. Mark Gilger to conduct clinical outcomes studies related to GI disorders in children using clinical registries and databases.

We are also examining the rate of management change after endoscopy for the evaluation of established IBD. Endoscopy is commonly performed in children with Inflammatory Bowel Disease (IBD), although endoscopic remission is not a standard therapeutic endpoint. The utility of repeat endoscopy for the management of pediatric IBD has not been subject to investigation. Our aim is to examine several specific clinical and demographic features that are potential determinants of management changes after endoscopy in children with IBD. Our future goal is to examine endoscopic and histologic endpoints for pediatric IBD (e.g., mucosal healing). I am also involved in protocols examining the epidemiology of IBD and clinical trials in IBD.

I have used the PEDS-CORI endoscopy databases to detect trends in complications among pediatric endoscopies. The database has been used to generate a new hypothesis and examine the utility of endoscopy for various indications. PEDS-CORI has been valuable to generate preliminary data for prospective studies in endoscopy. We are planning further studies related to quality improvement in pediatric endoscopy using PEDS-CORI.

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Molecular Mechanisms of Liver Regeneration

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SUNDARARAJAH THEVANANTHER

Recent Publications


The primary research objective of my laboratory is to understand the molecular mechanisms of liver regeneration after injury. Liver insufficiency after surgical hepatic resection is one of the most serious problems associated with multiple liver derangements such as fatty liver, steatosis, cirrhosis, severe fibrosis, and alcoholic hepatitis, the conditions with impaired liver regeneration. Most notably, acute liver failure is a rapidly progressive disorder associated with high mortality rates. Currently, orthotopic liver transplantation is the primary mode of intervention in these patients. However, the applicability of transplantation to patients with acute liver failure is limited by the relative shortage of donor organs, such that many patients die of rapidly progressive multi organ failure before a donor liver becomes available. A clear understanding of the mechanisms that control hepatocyte proliferation should suggest better treatment options promoting liver regeneration in patients with fatal liver diseases.

Hepatocytes are highly differentiated cells and comprise approximately 80% of liver mass in the adult liver. Adult hepatocytes generally remain quiescent and rarely undergo cell division, but they retain the remarkable ability to undergo cell division and proliferation in response to acute or chronic injury. Despite intense investigations for the past several decades, the key factors that initiate cell cycle progression and proliferation in adult hepatocytes remain unknown. In recent years, extracellular ATP is emerging as an important signaling molecule influencing a variety of liver functions via activation of cell surface purinergic receptors. Our recent study in primary rat hepatocytes and 70% partial hepatectomy of adult rats reveal a new role for extracellular ATP as a hepatic mitogen. Our preliminary data in mice also suggest that extracellular ATP via the activation of P2 purinergic receptors activates multiple signaling intermediates within hepatocytes, especially the c-Jun N-terminal kinase (JNK), a key signaling cascade necessary for hepatocyte proliferation and liver growth.

The current efforts in the laboratory consist of a combination of pharmacological and genetic approaches to tease out the role of extracellular ATP and its cognate P2 purinergic receptors [metabotropic G-protein coupled (P2Y) and ligand gated ion channels (P2X)] in liver regeneration in response to injury. State-of the art molecular and cellular biological techniques are applied to identify the intracellular signaling intermediates important for the signal transduction from the cell-surface P2 purinergic receptors to nuclear events essential for hepatocyte proliferation. The knowledge gained by these studies will significantly advance our understanding of the role of extracellular ATP on hepatocyte cell cycle control and help identify potential new therapeutic targets within the liver, with implications in the management of several liver disorders.

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Microbiome and Probiotics

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JAMES VERSALOVIC

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 microarray-based 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 next-generation DNA sequencing, quantitative PCR and high density microarrays to study shifts in the 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 custom microarrays and 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.

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Early Nutritional Influences on Mammalian Developmental Epigenetics

Research in the Waterland laboratory aims to understand how nutrition and other environmental influences during prenatal and early postnatal development affect individual susceptibility to various diseases later in life. Dr. Waterland’s group focuses on nutritional influences on developmental epigenetics as a likely mediating mechanism. Epigenetic mechanisms regulate tissue-specific patterns of gene expression and are established during development. DNA methylation is of particular interest because mammalian one-carbon metabolism, which supplies the methyl groups for DNA methylation, is intimately dependent on dietary methyl donors and cofactors. One question currently being explored is whether methyl donor nutrition during fetal and early postnatal development can permanently alter DNA methylation in the colonic epithelium and thereby affect lifelong susceptibility to colon cancer. The Waterland group is also increasingly interested in understanding the role of epigenetic dysregulation in obesity. In particular, they are studying whether maternal obesity and nutrition before and during pregnancy affect developmental epigenetics in the hypothalamus and, consequently, body weight regulation in the next generation. The Waterland group uses genome-wide DNA methylation profiling techniques, bisulfite pyrosequencing, and gene expression assays to study epigenetic regulation in mouse models and humans.

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Recent Publications


Targeting Chronic Diseases by Botanicals
Prevention of Childhood Obesity

WILLIAM W. WONG

Recent Publications


My research interests focus on studies of dietary supplementation for the prevention of chronic diseases and on programs for the prevention and treatment of childhood obesity.

In a multi-center, 2-year follow-up, randomized, double blind, and placebo-controlled study, 403 healthy postmenopausal women were assigned to receive a placebo, 80 mg/day or 120 mg/day of soy isoflavone supplementation for two years. The study showed that soy isoflavone supplementation at 120 mg/day had protective effect on whole-body bone mineral density with minimal risk. In a separate clinical trial, soy isoflavone supplementation at 80 mg/day stimulated nitric oxide production in postmenopausal women with high-normal blood pressure to stage 1 hypertension. Areas of future focus will include the potential health benefits of botanicals against cardiovascular disease and diabetes.

Currently, I am evaluating a summer camp program for the treatment of childhood obesity. Next year, I will be heading a multi-disciplinary, community-based program for the treatment of childhood obesity among minority children. The 4-year project, “Healthy Kids-Houston: An Integrated Program for the Prevention of Obesity among Minority Children,” will be funded by the United States Department of Agriculture. The project will involve strong partnership among Baylor College of Medicine, Texas Children’s Hospital, Texas Children’s Pediatric Associates, Houston Parks and Recreation Department, and the Houston Metropolitan Transist Authority. I will continue to explore the effectiveness of school-based and other community-based programs as well as the effectiveness of video games for the prevention and treatment of childhood obesity.

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Molecular Genetic Approaches to Cell Specification and Degeneration

HUDA Y. ZOGHBI

Professor
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Baylor College of Medicine

Recent Publications


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 Math1 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.

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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, hematology-oncology, infectious diseases, neonatal-perinatal medicine, nephrology, pulmonology, and rheumatology. Each candidate must be familiar with specific subspecialty training requirements as well as the policies stated in the current 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 Web site. All applicants 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. Individuals registered for a general pediatrics certifying examination may apply for a pediatric subspecialty certifying examination pending notification of results. Contact the ABP for details.

B. Licensure

An applicant must have a valid (current), unrestricted license to practice medicine in one of the states, districts, or territories of the United States or a province of Canada in which he or she practices or have unrestricted privileges to practice medicine in the US Armed Forces. 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.

An applicant who is practicing exclusively abroad may be exempted from this license requirement upon presentation of proof of licensure in the country in which he or she practices. A copy of the license must be submitted. In addition, applicants who practice or plan to practice exclusively abroad must submit a letter stating this fact.

C. Verification of Training

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 completion of 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 that full credit be provided for the marginal 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.

Appeals Process: 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.

Transfer of Fellowship Training: For continuity of training experiences, mentoring, and assurance of meeting training requirements, it is best that a Fellow complete all training in the same program. Occasionally, a Fellow may need to transfer to another program for compelling reasons. In such circumstances, it is incumbent that the program directors of the current program and the proposed program 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. For those Fellows beginning training July 1, 2004, and thereafter, 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.

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 (eg, 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/research during Fellowship training, but the current requirement has been modified to accommodate 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 (as outlined in Section F below).

Fellows who began training before July 1, 2004, who had an interruption in training or off-cycle dates and who had a Scholarship Oversight Committee in place for at least 24 months may qualify for the requirement for Scholarly Activity. Contact the ABP for additional information regarding this exception.

The program director is responsible for notifying all Fellows of the scholarly activity/research requirements necessary for certification upon entry to the subspecialty training program. Furthermore, in the description of the candidate’s scholarly activity or research 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 or research is based.

E. Principles Regarding the Assessment of Scholarly Activity (for those who began training July 1, 2004, and thereafter)
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, ie, 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, which is downloadable directly from the ABP's Web site.

F. **Principles Regarding the Assessment of Meaningful Accomplishment in Research**  
*(for those who began training prior to July 1, 2004)*

Evidence of meaningful accomplishment in research must be submitted, including one or more of the following:

- First author of a hypothesis-driven research paper accepted for publication in a peer-reviewed journal deemed acceptable by the Subboard. A reprint of the paper, or a copy of the letter of acceptance by the journal and a copy of the manuscript, must be submitted. This paper should be a product of the Fellowship training.
- A Ph.D. degree in a field of science. A copy of the degree certificate must be provided.
- A thesis accepted as partial fulfillment of the requirements for a postgraduate degree in a field relevant to the subspecialty. The thesis or a research progress report as described in (e) must be submitted for review with documentation that the thesis was accepted and/or the degree awarded.
- First author of a hypothesis-driven research paper that has been submitted but not yet accepted for publication in a peer-reviewed journal deemed acceptable by the Subboard. A letter and/or electronic communication from the journal confirming the receipt of the manuscript must be included, as well as a copy of the submitted manuscript.
- A research progress report (signed by both the applicant and mentor) no more than five pages in length that must include (a) a statement of hypothesis, (b) delineation of methodology, (c) results and analysis, and (d) significance of the research. A research progress report may not be used to meet the requirement if an applicant is more than 2 years beyond completion of Fellowship training unless there are extenuating circumstances that may have prevented submission of a manuscript.
Program Requirements for Residency Education in the Subspecialties of Pediatrics

Program Requirements for Residency Education in the subspecialties of pediatrics are approved by the ACGME or by the RCPSC. Program Requirements and a listing of accredited programs may be found on the ACGME web site: www.acgme.org, or the Royal College of Physicians and Surgeons of Canada’s web site: rcpsc.medical.org.

Training Leading to Dual Pediatric Subspecialty Certification

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.

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. This petition 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 Web site.

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 prospectively submitted 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.

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 degree 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 Subboard to waive the research requirements or, for those beginning subspecialty training July 1, 2004, and thereafter, 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 (e.g., 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 Special Alternative Pathway would not be eligible for subspecialty fast-tracking.

A subspecialty fellow who receives a waiver by the Subboard 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 accredited training in order to apply for certification. The full policy can be found on the ABP Web site.
The 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 must be fulfilled to be eligible for certification.

ADMISSION REQUIREMENTS
Physicians who entered training in pediatric gastroenterology on or after January 1, 1996, are required to complete their training in a program accredited for training in pediatric gastroenterology by the RC for Pediatrics in the United States or the RCPSC in Canada.
A subspecialty Fellow who entered pediatric gastroenterology training before January 1, 1990, may apply for admission on the basis of completion of 2 years of Fellowship training in pediatric gastroenterology. Only those pediatric gastroenterology training programs that were operated in association with general comprehensive pediatric residency programs accredited by the RC or by the RCPSC are acceptable. Three years of full-time, broad-based Fellowship training in pediatric gastroenterology are required for Fellows entering training on or after January 1, 1990. No continuous absence of more than 1 year will be permitted. Combined absences/leave in excess of 3 months during the 3 years of training, whether for vacation, parental leave, illness, etc, must be made up. If the program director believes that combined absences/leave that exceeds 3 months is justified, a letter of explanation should be sent by the director for review by the Credentials Committee.
For a Fellow who began pediatric gastroenterology training on or after January 1, 1990, 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 either the criteria stated in the "Principles Regarding the Assessment of Scholarly Activity" or the criteria stated in the "Principles Regarding the Assessment of Meaningful Accomplishment in Research" as described in the General Criteria for Certification in the Pediatric Subspecialties. Fellows who began training after July 1, 2004, must meet the requirements for scholarly activity;
- The Fellow must pass the subspecialty certifying examination
A Fellow beginning part-time training after January 1, 1990, may complete the required training on a part-time basis not to exceed 6 years.

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.