



# Honoring the Past, Shaping the Future.

75 YEARS OF DISCOVERY, INNOVATION AND CARE



Division of Gastroenterology and Hepatology

UNIVERSITY OF MICHIGAN HEALTH SYSTEM





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## Welcome

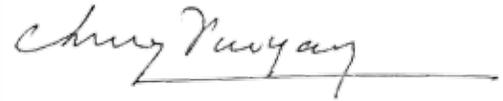
The world was a different place 75 years ago, when the nascent Division of Gastroenterology and Hepatology began. A new car cost \$850, and gas was 12 cents a gallon. Thanksgiving had just become an official national holiday. *The Maltese Falcon* was one of the most popular movies and "Chattanooga Choo-Choo" one of the most popular songs. And the massive presidential sculptures on Mount Rushmore were unveiled.

But while much has changed, some things remain constant, including our commitment to excellence in patient care.

As you read through these pages, you'll find the history of our Division in words and images. From the earliest days of the first Division Chief H. Marvin Pollard, who introduced the fiberoptic endoscope, to this year's brand-new innovations in research and clinical care, the Division has remained true to its mission of finding new solutions for clinical issues and developing and training the next generation of leaders.

We've done great work, and we've had fun doing it. As one former faculty member put it, "There are very few academic departments in any university in the world with this much talent, and faculty who stay in harmony and love and respect each other."

Here's to the next 75 years of research and discovery!



**CHUNG OWYANG, MD**

pancreas





Liver

Stomach

**Foundations:** OUR HISTORY

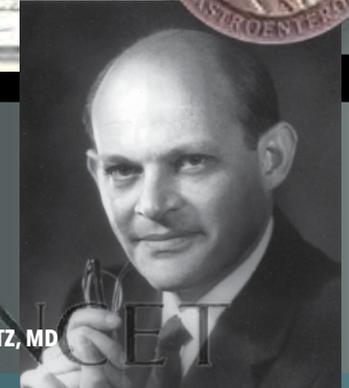
Small Intestine

Large Intestine



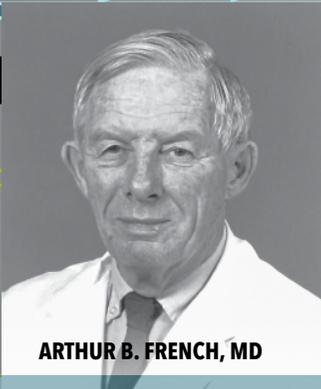
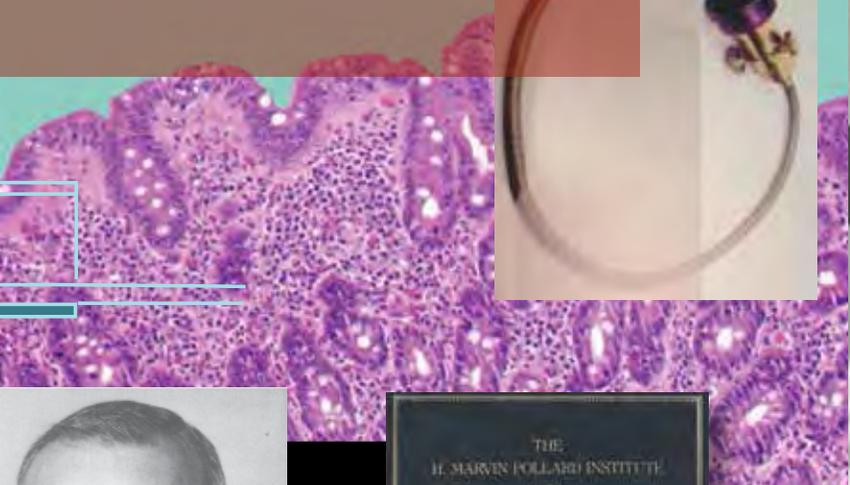
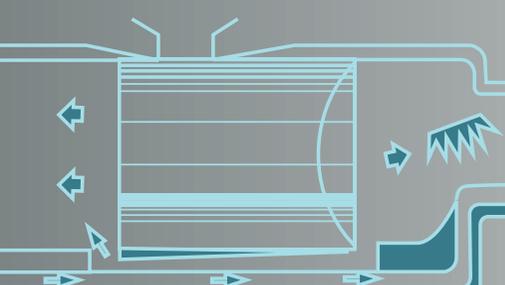
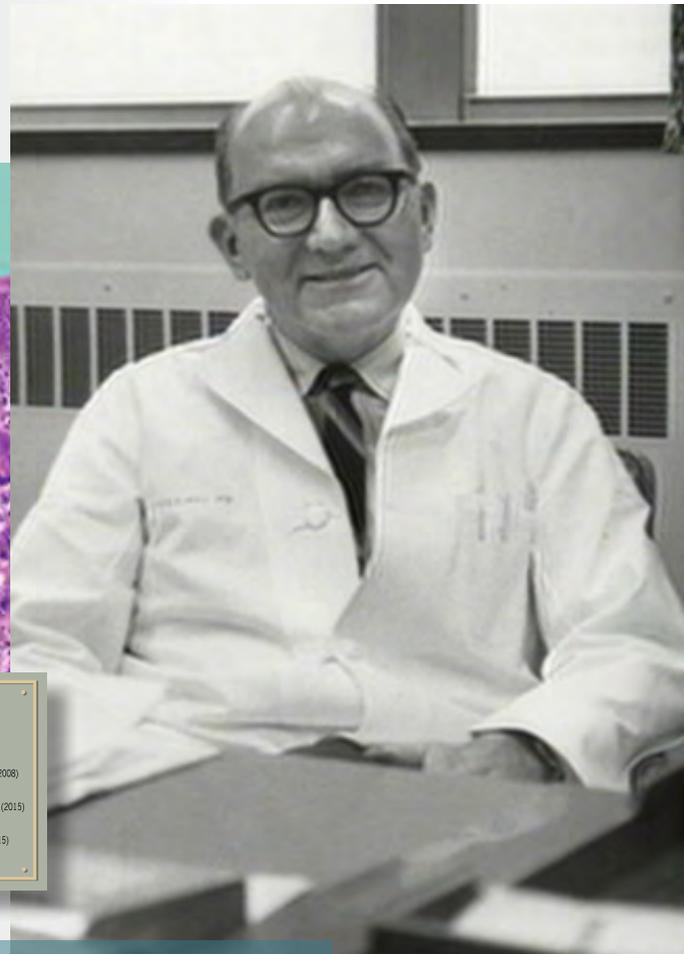
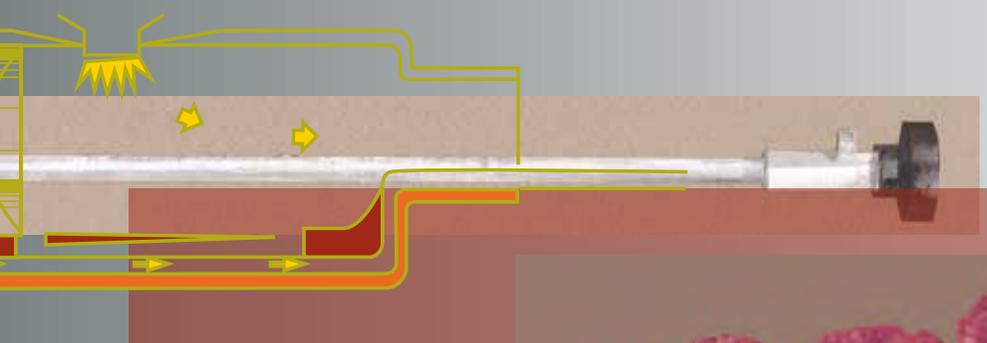


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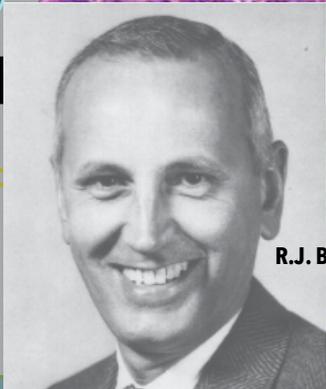


THE LANCET

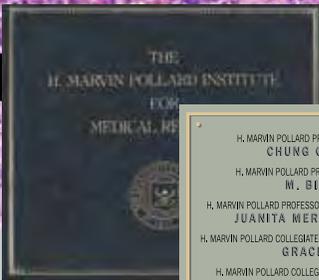
BASIL I. HIRSCHOWITZ, MD



**ARTHUR B. FRENCH, MD**



**R.J. BOLT, MD**



- H. MARVIN POLLARD PROFESSOR OF INTERNAL MEDICINE  
CHUNG OWYANG, M.D.
- H. MARVIN POLLARD PROFESSOR OF GASTROENTEROLOGY  
M. BISHR OMARY
- H. MARVIN POLLARD PROFESSOR OF GASTROINTESTINAL SCIENCES (2008)  
JANITA MERCHANT, M.D., PH.D.
- H. MARVIN POLLARD COLLEGIATE PROFESSOR OF GASTROENTEROLOGY (2015)  
GRACE ELTA, M.D.
- H. MARVIN POLLARD COLLEGIATE PROFESSOR OF ENDOSCOPY (2015)  
THOMAS D. WANG, M.D., PH.D.

**Dr. H. Marvin Pollard { Division Chief 1947 - 1972 }**

## The Pollard Era { 1940 - 1972 }



Under the leadership of **DR. H. MARVIN POLLARD** (MD 1931, Residency 1933), the University of Michigan Division of Gastroenterology was founded in the 1940s, long before the specialty was officially recognized by the American Board of Internal Medicine. Dr. Pollard attended a number of postgraduate courses, but he was not formally trained as a gastroenterologist. Still, he went on to become a renowned pancreatic cancer researcher, a visionary leader of the Division and an innovative thinker. With characteristic foresight, he laid a strong foundation upon which the Division would continue to grow and flourish in clinical care, training and research.

Dr. Pollard was the first to introduce the fiberoptic endoscope, a semi-rigid endoscope, into the GI Division's clinics. He believed strongly in the importance of research to fuel innovation in clinical practice and that every prominent academic entity should devote considerable time and effort in pursuit of basic and clinical research. Since there were

no resources available at that time to fund such programs, Dr. Pollard undertook a fundraising effort, personally soliciting donors. He used the monies to help establish the first gastrointestinal research unit at the University of Michigan.

### A foundation for research excellence

The resulting Marvin Pollard GI Research Center represented a groundbreaking institution, the

first of its kind to receive National Institutes of Health research funding and career development awards. It remains in existence today and has played a significant role in many investigational efforts over the years as well as in attracting **TADATAKA "TACHI" YAMADA, MD, KBE**, to the University as Division Chief in 1983.

When Dr. Yamada and **DR. CHUNG OWYANG**, current Division Chief, applied to the NIH in the early 1980s to support an additional research center

focused on gastrointestinal peptides, the Pollard GI Research Institute helped demonstrate the Division's long history of and commitment to successful clinical and translational research. A grant to establish the new center was awarded, and the Center for Gastrointestinal Research is thriving and has been continuously funded since its founding in 1984.

During his tenure, Dr. Pollard trained a number of notable gastroenterologists, who went on to become prominent inventors, clinicians and leaders in their own right: **DRS. BASIL I. HIRSCHOWITZ, KEITH S. HENLEY, ROBERT J. BOLT, WILLIAM H. BACHRACH, ARTHUR B. FRENCH, LUDOVIC STANDAERT, JORGE GUMUCIO, MILTON WEISER and DAVID W. WATSON.**

### Invention and innovation

One of the most important developments during the Pollard era was Dr. Hirschowitz's invention of the fiberoptic endoscope, the first fully flexible scope able to examine the upper gut. Working together with renowned fiberoptics experts Drs. Hopkins and Kapany, and subsequently with U-M colleagues C. Wilbur Peters and undergraduate student Lawrence E. Curtiss of the Physics department, Dr. Hirschowitz completed construction of the first generation fiberscope, supported with resources provided by Dr. Pollard. The invention became the prototype for the gastroduodenal scope the Division now uses in its Medical Procedures Unit. For this achievement, Dr. Hirschowitz was awarded the

Julius Friedenwald Medal, the highest distinction bestowed by the American Gastroenterological Association.

An equally important achievement during the Pollard era was the development of a simplified multiple-retrieving small-bowel biopsy tube. In 1962, Drs. Bolt and French, who both trained under Dr. Pollard, performed the modern era's first intestinal biopsy. The three physicians published their invention and findings in *The American Journal of Digestive Diseases* (1962; 7: 773).

Using this instrument, Drs. French and Bolt performed pioneering studies correlating morphology and malabsorption in celiac disease. Subsequently, Dr. French went on to serve as the first director of the U-M Clinical Research Unit.

An inspiring mentor to his U-M colleagues and a masterful clinician with patients, Dr. Pollard also generously gave of his time to the profession. He presided over a number of organizations including the American Gastroenterology Association, the American College of Physicians and the American Cancer Society. He was also one of the founders of the World Gastroenterology Organisation and served as its president.

The endowments in Dr. Pollard's name have grown over the last 30 years and currently fully support seven endowed professorships within the Division of Gastroenterology. Dr. Pollard retired in 1972, after more than three decades leading the Division.

# 1st

Founder and first Division  
Chief of Gastroenterology  
(1940 - 1972)

President of AGA, ASGE, ACP,  
American Cancer Society

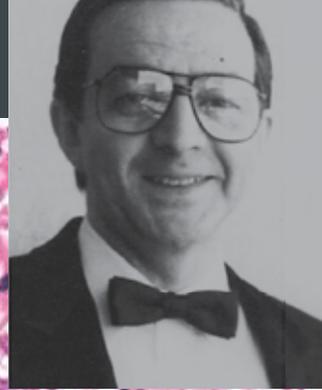
# 1st

Development of first fiberoptic  
gastroscope

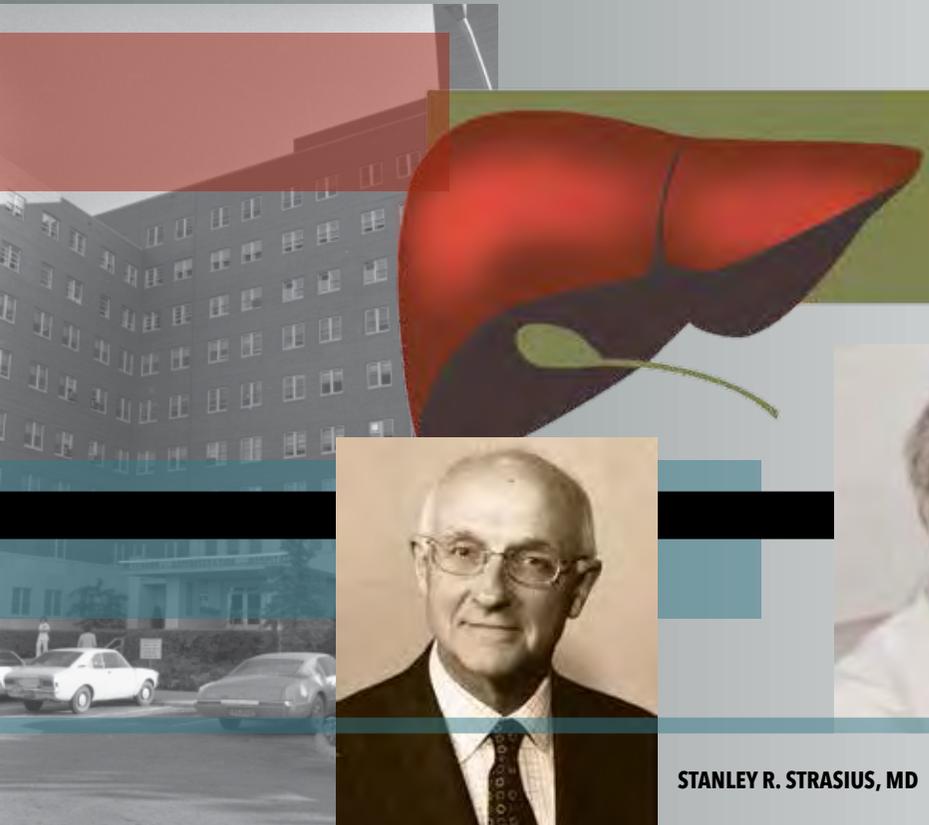
Renowned researcher in  
pancreatic cancer



**JORGE J. GUMUCIO, MD**



**MILTON G. MUTCHNICK, MD**



**STANLEY R. STRASIUS, MD**



**WILLIAM O. DOBBINS III, MD**



**Dr. Keith S. Henley { Division Chief 1972 - 1981 }**

## The Henley Era { 1972 - 1981 }



After Dr. Pollard retired in the fall of 1972, **DR. KEITH S. HENLEY**, a hepatologist interested in alcoholic liver disease, was appointed the second Chief of Gastroenterology. Dr. Henley quickly became known for his integrity, accessibility, scrupulous fairness and deep moral conscience.

Financial pressures in the late 1960s challenged Dr. Henley to continue to build a community of scholars in gastroenterology once he took over as chief. He devoted considerable effort to recruiting faculty capable of obtaining NIH grants in order to help rejuvenate the Division.

Together with **DRS. MILTON G. MUTCHNICK** and **JORGE GUMUCIO**, Dr. Henley developed a research group dedicated to the study of basic and translational hepatology.

Dr. Henley was able to attract budding GI talent, including current Division Chief **DR. CHUNG OWYANG**; **DR. TIMOTHY T. NOSTRANT**; **DR. JOEL V. WEINSTOCK** and **DR. JEANPIERRE RAUFMAN**, both of whom are now division chiefs at other institutions; **DR. JOHN A. SCHAFFNER**, who enjoys a distinguished career as an educator at the Mayo Clinic; and **DR. STANLEY R. STRASIUS**, who is a leading teacher at St. Joseph Mercy Hospital in Ann Arbor.

Dr. Henley also strengthened the GI presence at the Ann Arbor VA hospital and helped develop what would

become the U-M Liver Transplant Program, one of the first in the United States. The results of his clinical efforts and his hepatology research have had far-reaching impact on the care of liver disease and liver transplant patients.

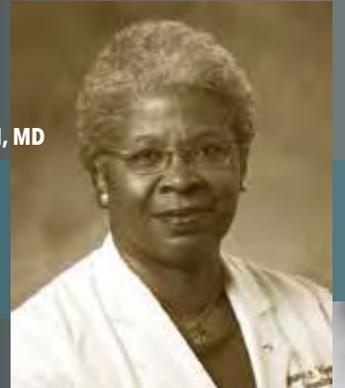
Dr. Henley led the Division until 1981 and retired in 1993.



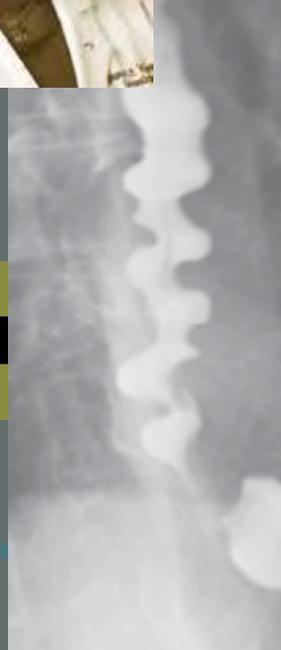
Dr. Chung Owyang with Dr. Henley (1979)



JOANNE WILSON, MD



DR. NOSTRANT WITH DR. WILLIAM D. CHEY



**M**  
**MEDICAL SCHOOL**  
 UNIVERSITY OF MICHIGAN

James O. Wooliscroft, M.D.  
 Dean, D-R Medical School  
 Lyle C. Roll Professor of Medicine

cordially invites you to the inauguration of the

**Timothy T. Nostrant, M.D.**  
 Collegiate Professorship in Gastroenterology

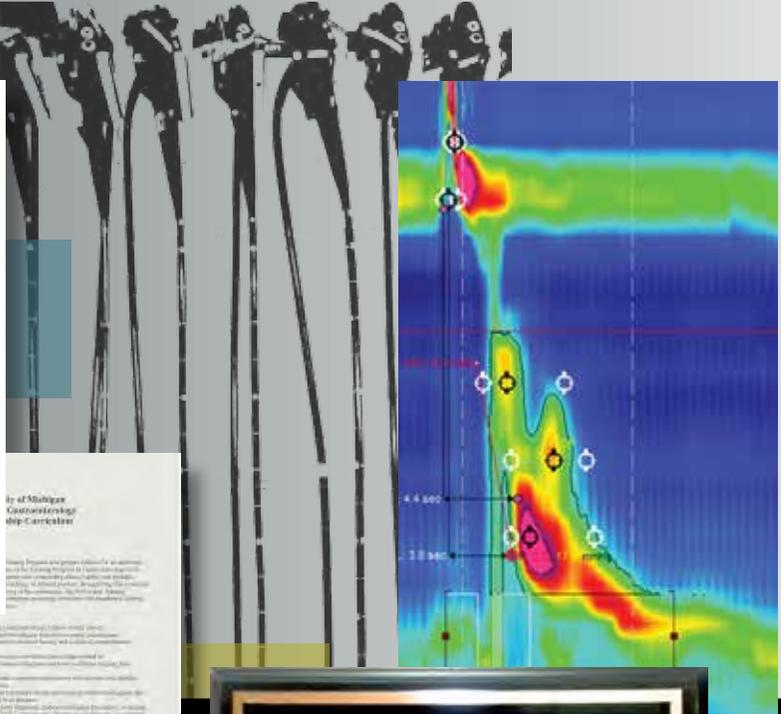
Friday, March 13, 2015

5:00 p.m. Ceremony  
 D. Dan and Betty Kahn Auditorium

6:00 p.m. Reception  
 6:45 p.m. Dinner  
 Gilbert S. Dinwiddie Atrium

A. Alfred Taubman Medical Science Research Building  
 109 Zina Pilsner Place  
 Ann Arbor

Please reply by Thursday, March 5  
 to Dawn Redman: [eredman@umich.edu](mailto:eredman@umich.edu) or 734-763-5099



**A. Alfred Taubman Medical Science Research Building**  
 109 Zina Pilsner Place  
 Ann Arbor

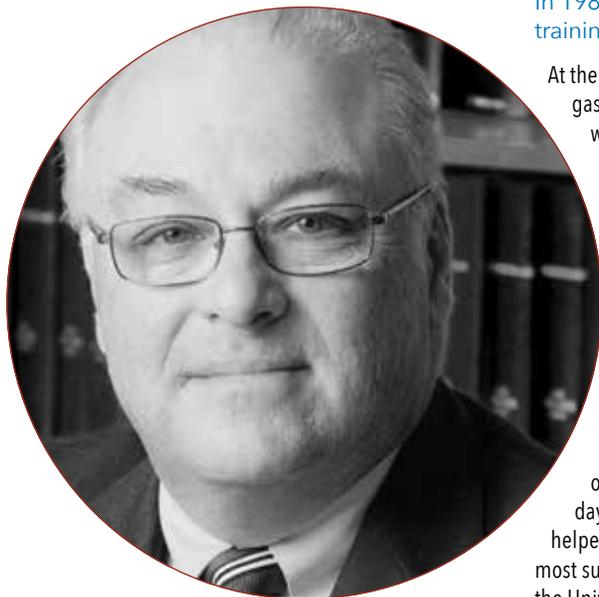
Please reply by Thursday, March 5  
 to Dawn Redman: [eredman@umich.edu](mailto:eredman@umich.edu) or 734-763-5099

**Timothy T. Nostrant, M.D.**  
 Fellows Room



**Dr. Timothy T. Nostrant { Division Chief 1981 - 1983 }**

## The Nostrant Era { 1981 - 1983 }



In 1981, **DR. TIMOTHY T. NOSTRANT**, then an assistant professor who had completed his GI fellowship training at the University of Michigan, was appointed acting chief following Dr. Henley.

At the time, the nature of gastroenterology was changing with the advancements brought by endoscopy technology. Dr. Nostrant recognized the importance and potential of endoscopy, and he was instrumental in establishing one of the world's most sophisticated and well-equipped medical procedures units (MPU) to expand the use of the technology. To this day, the MPU that Dr. Nostrant helped create remains one of the most successful clinical units in the University of Michigan Health

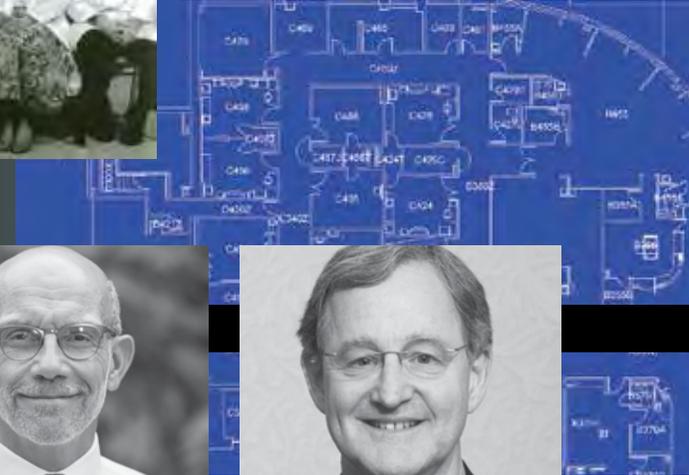
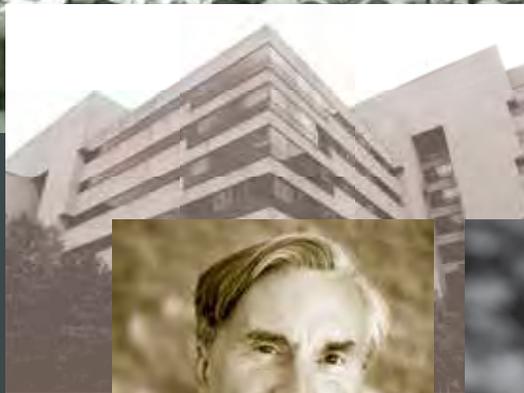
System (UMHS), with over 30,000 procedures performed in 2016 alone.

Dr. Nostrant made significant contributions to the field of esophageal motility disorders and trained many of the key clinical faculty members in the Division. He developed the core curriculum for the Gastroenterology Fellowship Program, much of which is still in use today.

Dr. Nostrant also served as the lead physician of the Department of Internal Medicine's Faculty Diagnostic Unit, which was designed to be a national model for the development of the clinician scholar track of academic medicine. Within a relatively short time, Dr.

Nostrant built this unit into one of the most productive and sought-after consultative services in the Department. Its multi-subspecialty approach to consultation has served as a blueprint for other departments across the UMHS.





**RICHARD H. MOSLEY, MD**



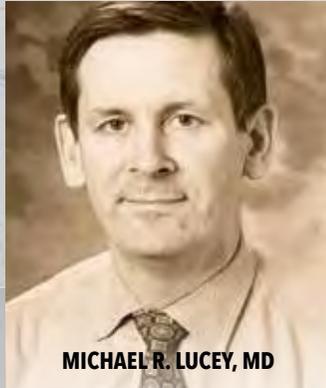
**JOHN DEL VALLE, MD**



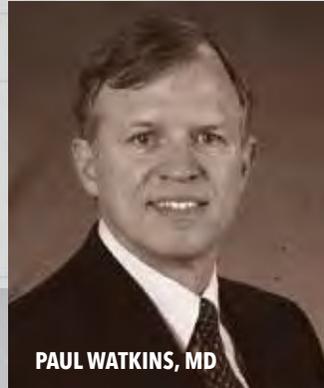
**C. RICHARD BOLAND, MD**



**REBECCA W. VAN DYKE, MD**



**MICHAEL R. LUCEY, MD**



**PAUL WATKINS, MD**



**Dr. Tadataka "Tachi" Yamada { Division Chief 1983 - 1990 }**

## The Yamada Era { 1983 - 1990 }



In 1983, **DR. TADATAKA "TACHI" YAMADA** joined the University of Michigan as Chief of Gastroenterology—selected for his unique potential, vision and drive, despite the fact that he was a relatively young researcher at the time.

When Dr. Yamada assumed the role of Division Chief, the Division had just seven full-time faculty members and a single NIH research grant. Dr. Yamada saw this as a tremendous opportunity. His first major initiative was to write a highly multi-disciplinary—and winning—proposal for a National Institutes of Health Digestive Diseases Center grant, which was crucial in establishing the University of Michigan Center for Gastrointestinal Research, the first center in the United States dedicated to the investigation of gut peptides.

The Center provided the infrastructure for Dr. Yamada to build one of the strongest GI research programs in the country, and it played a key role in the recruitment of **DR. JOHN WILLIAMS** to the Division as well as **DR. BISHR OMARY** to the Chair of Physiology and **DR. JACK DIXON** to the Chair of Biological Chemistry.

Dr. Yamada was a true pioneer in gut endocrinology. He was among the earliest investigators to apply molecular biology techniques to the study of biochemistry and physiology of gut hormones. He made a number of novel contributions vital to our understanding of the synthesis, release and actions

of these hormones. His first major breakthrough was the development of an isolated cell system to study the regulation of peptide secretion from gastrointestinal endocrine cells. Until the introduction of this technology, it was virtually impossible to study the cell biology of gut hormones because they are contained in cells dispersed throughout the mucosa, rather than isolated within endocrine glands.

Another equally important contribution was the isolation and characterization of glycine-extended processing intermediates of gastrin, which provided tools of critical importance in the biological activation

of nearly 50 percent of all known peptide hormones. Many of Dr. Yamada's observations have clinical implications as fundamental tools for understanding the pharmacology of histamine receptor antagonists and serve as the basis of important pharmacological interventions for health problems such as obesity.

As Chief, Dr. Yamada had a gift for bringing scientists from different backgrounds together and fostering deep collaborations in pursuit of groundbreaking research. He recruited a number of promising young physician-scientists to the Division. These include **DRS. RICHARD BOLAND, RICHARD MOSELEY, PAUL WATKINS** and **REBECCA VAN DYKE**.

Dr. Boland served as Section Chief of the VA Ann Arbor Healthcare System and, subsequently, as Division Chief at University of California, San Diego. Dr. Moseley succeeded Dr. Boland as VA Section Chief and subsequently was appointed Chief of Medicine of the VA Ann Arbor Healthcare System. Dr. Watkins is a renowned expert in liver drug toxicity and served as director of the clinical research center at U-M. He now directs the Hamner-University of North Carolina Institute for Drug Safety Sciences. Dr. Van Dyke became Professor of Medicine at U-M, contributing significantly to the Division's medical education mission and earning many awards for her teaching and mentorship. She was named professor emerita in 2014.

Dr. Yamada is also known for helping junior faculty launch their careers and realize their potential. Many of the faculty members he trained have gone on to become academic leaders in gastroenterology and hepatology. **DR. PETER TRABER** became Chair of the Department of Internal Medicine and subsequent Dean of Medicine at the University of Pennsylvania, and also served as president of Baylor College of Medicine.

**DR. CHRIS DICKINSON** has served as Chief of Pediatric Gastroenterology at U-M for many years and is now Chief Clinical Officer of the C.S. Mott Children's Hospital and the Von Voigtlander Women's Hospital. **DR. JOHN DEL VALLE**, a former Robert Wood Johnson trainee, now serves as Associate Chair of Medicine and Director of the

Medicine and MED-Peds Residency Programs at U-M. **DR. GRACE ELTA**, H. Marvin Pollard Collegiate Professor of Gastroenterology, directs the U-M Medical Procedures Unit. She was the first woman to serve on the governing board of the American Gastroenterological Association and served as the first female president of the American Society for Gastrointestinal Endoscopy. **DR. JUANITA MERCHANT**, endowed Professor of Medicine, directs a thriving, internationally renowned research program on transcriptional control mechanisms in the gastrointestinal tract. **DR. JAMES SCHEIMAN** is Professor of Medicine and directs the Advanced Endoscopy Fellowship program at U-M. **DR. MICHAEL LUCEY**, an expert in liver transplant, serves as Chief of Gastroenterology and Hepatology at the University of Wisconsin.

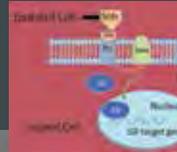
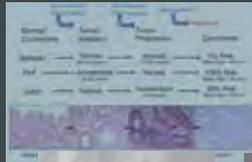
Many foreign fellows mentored by Dr. Yamada also have gone on to achieve significant academic success. Dr. Kentaro Sugano is Chair of Medicine at Jichi University, and Dr. Tsutomu Chiba is Chair of Medicine at Kyoto University, both in Japan.

During Dr. Yamada's tenure, annual research funding increased from about \$200,000 to \$4 million, setting the stage for the \$15 million in funding the Division generated in 2016.

Another major achievement for Dr. Yamada was editing the *Textbook of Gastroenterology*, one of the most-used GI textbooks to date. It is considered a standard GI textbook both in the U.S. and worldwide. It is currently in its 6th edition.



Editors of *Textbook of Gastroenterology*: Don W. Powell, Chung Owyang, Tadataka Yamada, Fred E. Silverstein, David H. Alpers



**JOHN M. CARETHERS, MD**



**JUANITA L. MERCHANT, MD, PhD**



**JOSEPH C. KOLARS, MD**



**WILLIAM L. HASLER, MD**



**FRED ASKARI, MD, PhD**



**HARI CONJEEVARAM, MD, MSc**



**GRACE ELTA, MD**



**LESLIE B. ALDRICH, MD**



**GRACE SU, MD**



**JAMES M. SCHEIMAN, MD**

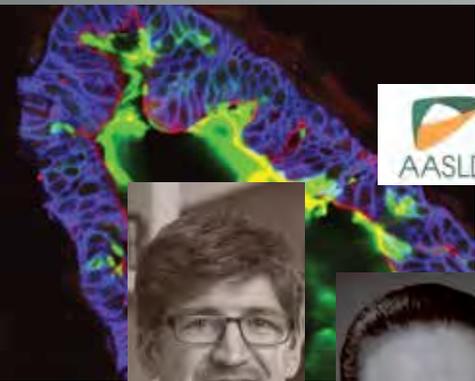


**JOHN W. WILEY, MD**



**PETER D.R. HIGGINS, MD, PhD, MSc**





**JOHN R. SPENCE,  
PhD**



**ELIZABETH K.  
SPELIOTES, MD,  
PhD, MPH**



**ANNA SUK-FONG  
LOK, MD, FRCP**



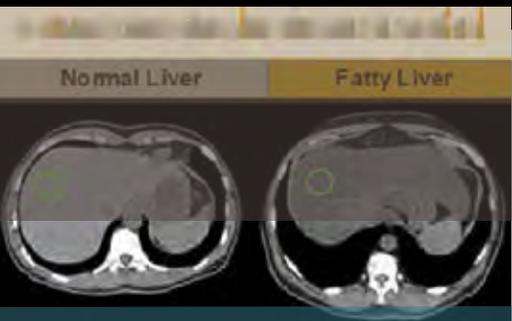
**ROBERT J.  
FONTANA, MD**



**WILLIAM D. CHEY,  
MD**



**M. BISHR OMARY  
MD, PhD**



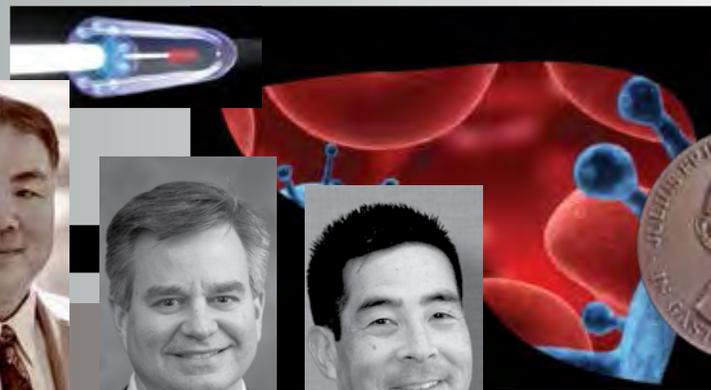
**THOMAS D. WANG,  
MD, PhD**



**PHILIP S.  
SCHOENFELD, MD,  
MSED, MSc**



**JOHN M.  
INADOMI, MD**



**Dr. Chung Owyang { Division Chief 1990 - Present }**

## The Owyang Era { 1990 - Present }



In 1990, **DR. TACHI YAMADA** became Chair of Internal Medicine and **DR. CHUNG OWYANG** was appointed Chief of Gastroenterology and Hepatology. Dr. Owyang brought his energy and vision to strengthen the Division's accomplishments.

Like Dr. Yamada, Dr. Owyang is also a gut endocrinologist. His work focuses on the neuronal hormone control of digestive functions in pancreatic exocrine secretion and GI motility. One of his major achievements is the characterization of a trypsin-sensitive CCK-releasing factor, which is secreted in the intestinal lumen following feeding. This novel observation has provided the basis for understanding the clinical utility of pancreatic enzyme supplements in alleviating pain in chronic pancreatitis. Dr. Owyang also studied the *in vitro* action of somatostatin on the enteric

nervous system and was the first to propose the use of somatostatin in the treatment of intestinal pseudoobstruction. His research work has been continuously funded by the NIH over the last 30 years.

As Division Chief, one of Dr. Owyang's first initiatives was to establish a clinical hepatology unit, recruiting **DR. ANNA LOK**, an expert in viral hepatitis, as its director. Under her leadership, the Division groomed many leading hepatologists, including **DR. ROBERT J. FONTANA**, Director of the University of Michigan Liver Transplant Program and Transplant Hepatology Fellowship Program; **DR. JORGE MARRERO**, leader of our nationally designated liver cancer program; **DR.**

**HARI CONJEEVARAM**, leading expert in non-alcoholic fatty liver disease and Director of the Gastroenterology and Hepatology Fellowship Training Program; **DR. FRED ASKARI**, Director of the nationally recognized Center of Excellence in Wilson Disease; and **DR. GRACE SU**, Chief of Gastroenterology at the VA Ann Arbor Healthcare System.

Dr. Owyang also fortified the Division's strength in health services research, recruiting **DRS. PHILIP SCHOENFELD** and **JOHN INADOMI**, who helped the Division secure highly competitive NIH T32 training grants in clinical epidemiology and outcomes research.

Dr. Owyang established one of the country's most comprehensive motility disorder groups, which includes **DRS.**

**JOHN WILEY** (visceral hypersensitivity and IBS), **WILLIAM D. CHEY** (food allergy and IBS), **WILLIAM HASLER** (gastroparesis), Philip Schoenfeld (outcomes research and functional bowel disorders), **RICHARD SAAD** (pelvic floor disorders and colonic inertia), **SHANTI ESWARAN** (IBS) and **JOEL RUBENSTEIN** (esophageal motility disorders, reflux and Barrett's Esophagus). Dr. Owyang's own research has focused on intestinal pseudo-obstruction, microbiome and IBS.

In 2000, Dr. Owyang oversaw the transformation of the Michigan Gastrointestinal Peptide Research Center into the University of Michigan Center for Gastrointestinal Research. More than 75 faculty from Gastroenterology and Hepatology, Physiology, Cell Biology, Microbiology, Pharmacology and Surgery galvanized the efforts of the established group of gut peptide in-

investigators. The Center is now a pillar of the Division, promoting academic development and fueling recruiting efforts for the Division and across the Department of Internal Medicine.

With Center support, several key NIH-funded research programs were developed. Collaborating with **DRS. DEBORAH GUMUCIO, LINDA SAMUELSON** and **ANDREA TODISCO, DR. JUANITA MERCHANT** initiated a novel program to study cellular decisions of differentiation in the GI tract, showing that Hedgehog pathology mediates the transition from inflammation to cancer in the GI tract.

The Center also was instrumental in recruiting **DR. THOMAS WANG**, a physician scientist and biomedical engineer whose molecular imaging techniques elucidate gene and protein expression. Center investigator **DR. ELIZABETH SPELIOTES** uses

human population-based studies and functional genomics to determine the genetics of obesity and fatty liver disease. **DR. JASON SPENCE**, a developmental biologist, creates three-dimensional organoid models to study intestinal stem cells. **DR. PETER HIGGINS**, who directs our inflammatory bowel disease program, established the Division's Biospecimen Banking Service to facilitate the translation of basic discoveries in cell lines and mouse models to human applications.

The Division continues to train the next generation of physicians. Many graduates of our GI Fellowship Training Program have become academic leaders in their own right. Notables include U-M Chair of Internal Medicine **DR. JOHN CARETHERS**; **DR. JOSEPH KOLARS**, senior associate dean of medicine; and **DR. WILLIAM D. CHEY**, professor and

director of the GI Physiology Laboratory. **DR. ELLEN ZIMMERMAN** went on to serve as associate chair of medicine at the University of Florida and **DR. URI LADABAUM** serves as acting chief of gastroenterology at Stanford University.

During his tenure, Dr. Owyang has greatly expanded the Division's clinical services and outreach programs. By 2016, with a clinical practice involving more than 75 full-time faculty, the Division became the second largest digestive and liver health group in the nation.

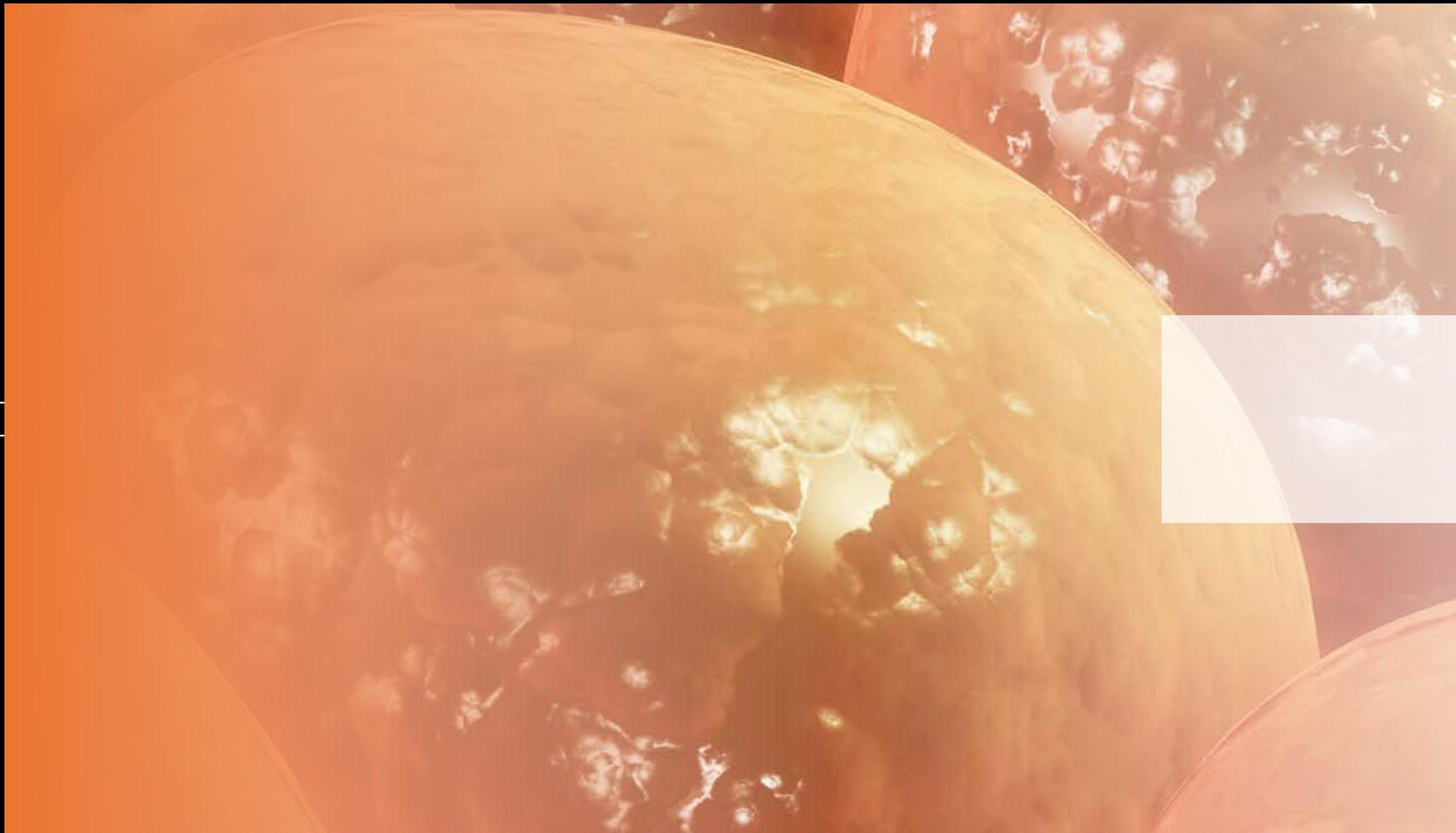
Under the leadership of **DR. GRACE ELTA**, the Medical Procedures Unit has become a hub for all major endoscopy procedures. A second Medical Procedure Center was opened in 2005 at the East Ann Arbor Health Campus and, under the direction of **DR. LESLIE ALDRICH**, has performed over 9,000 procedures in 2016. The

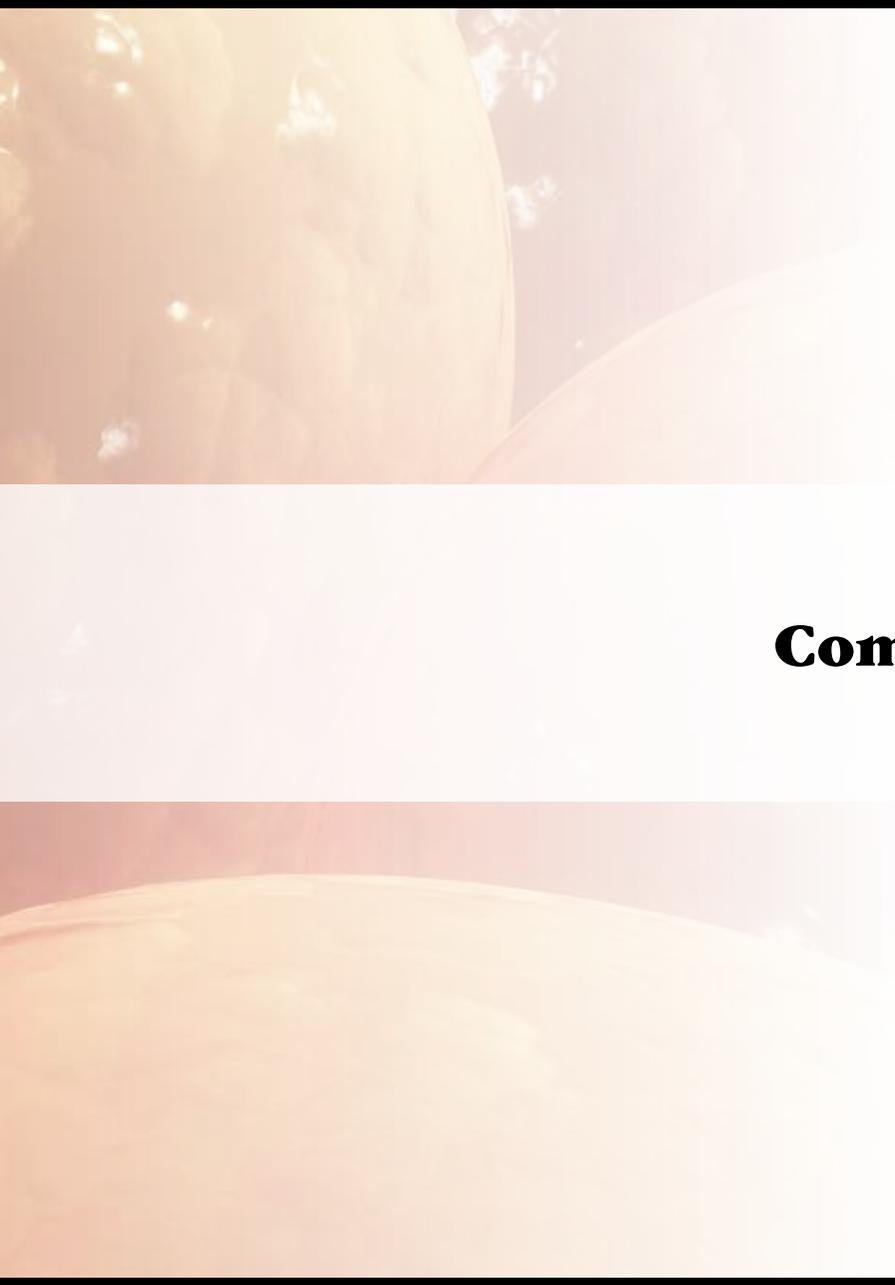
Division's clinical services encompass 14 locations and four endoscopy centers across Michigan. As of 2016, the Division had over 41,000 outpatient clinic visits and performed more than 30,000 procedures.

With nearly \$15 million of NIH funding each year, Division scientists and clinicians work side by side to provide the most advanced and innovative treatment options and care. Our Digestive and Liver Health Center is now a preferred referral center throughout Michigan and the world. The Division has housed *The American Journal of Gastroenterology and Gastroenterology*, with **DRS. BISHR OMARY** and **WILLIAM D. CHEY**, respectively, serving as editors-in-chief.

Many faculty have emerged as world leaders in gastroenterology and hepatology. In 2013, the American Gastroenterology Association (AGA)

bestowed the Julius Friedenwald Medal, its highest honor, upon Dr. Owyang for his lifelong contributions to the field of gastroenterology. In the last 50 years, two of our Division Chiefs—**DRS. YAMADA** and **OWYANG**—have been awarded this honor. **DRS. TIMOTHY NOSTRANT, GRACE ELTA**, and **WILLIAM D. CHEY** have received the AGA Distinguished Clinician Award. The AGA Distinguished Educator Award was given to **DRS. JOHN DEL VALLE** and **JOSEPH KOLARS. DR. ANNA LOK** has received several awards for her work, including the prestigious AGA William Beaumont Prize in Gastroenterology in 2016. These awards represent only a fraction of the enormous accomplishments of our faculty over the past 75 years.





**Committed to Excellence**

# **Faculty Leadership**

## Current Faculty Members

The faculty is the most valuable resource of the Division. Special emphasis is placed on faculty mentoring and career support. Each junior faculty (clinical lecturer and assistant professor) member is assigned a mentorship committee which meets quarterly and a career plan and timeline are carefully mapped out. As a result, an 80 percent success rate was achieved in obtaining career development awards.

**MEGAN ADKINS ADAMS**  
Lecturer

**LESLIE BROWN ALDRICH**  
Assistant Professor

**JOHN IRVIN ALLEN**  
Professor

**MICHELLE A. ANDERSON**  
Associate Professor

**FREDERICK K. ASKARI**  
Associate Professor

**ALLAN BARBISH**  
Instructor

**SHRINIVAS BISHU**  
Assistant Professor

**JOHN M. CARETHERS**  
Professor

**CRISTINA CEBRIAN LIGERO**  
Lecturer

**JOAN CHEN**  
Lecturer

**WILLIAM D. CHEY**  
Professor

**HARI S. CONJEEVARAM**  
Professor

**HOWARD C. CRAWFORD \***  
Professor

**DUYEN DANG**  
Associate Professor

**JOHN DEL VALLE**  
Professor

**MATTHEW J. DIMAGNO**  
Assistant Professor

**MOHAMAD EL ZAATARI**  
Research Investigator

**BADIH JOSEPH ELMUNZER**  
Adjunct Assistant Professor

**GRACE H. ELTA**  
Professor

**SHANTI L. ESWARAN**  
Assistant Professor

**LAUREL R FISHER**  
Associate Professor Emeritus

**ROBERT JOHN FONTANA**  
Professor

**MERRITT G. GILLILLAND III**  
Research Investigator

**LISA M. GLASS**  
Lecturer

**SHAIL GOVANI**  
Lecturer

**GINTAUTAS GRABAUSKAS**  
Assistant Research Scientist

**TANNAZ GUIVATCHIAN**  
Adjunct Lecturer

**DEBORAH L. GUMUCIO \***  
Professor

**WILLIAM LEE HASLER**  
Professor

**TADD HIATT**  
Lecturer

**PETER DOYLE HIGGINS**  
Associate Professor

**SHUANGSONG HONG**  
Assistant Research Scientist

**AMY HOSMER**  
Lecturer

**NOBUHIKO KAMADA**  
Assistant Professor

**JOHN Y. KAO**  
Associate Professor

**ALBERT C KIM**  
Lecturer

**JAMI KINNUCAN**  
Lecturer

**MINORU KOI**  
Associate Research Scientist

**JOSEPH C. KOLARS**  
Professor

\* Joint Appointment

**MONICA A. T. KONERMAN**

Lecturer

**JACOB E. KURLANDER**

Lecturer

**HELLAN KANG KWON**

Assistant Professor

**RICHARD S. KWON**

Assistant Professor

**RYAN J. LAW**

Lecturer

**ALLEN LEE**

Lecturer

**HAIJUN LI**

Research Investigator

**JI-YAO LI**

Assistant Research Scientist

**ANNA SUK-FONG LOK**

Professor

**COSTAS ANDREAS LYSSIOTIS \***

Assistant Professor

**JOHN C. MAGEE \***

Professor

**BETH ROSE MANOOGIAN**

Assistant Professor

**JESSICA MELLINGER**

Lecturer

**STACY B. MENEES**

Assistant Professor

**JUANITA L. MERCHANT**

Professor

**RICHARD H. MOSELEY**

Professor Emeritus

**MICHELLE M. MUZA-MOONS**

Lecturer

**BORKO NOJKOV**

Lecturer

**BISHR OMARY \***

Professor

**CHUNG OWYANG**

Professor

**AARTI OZA BEDI**

Lecturer

**NEEHAR PARIKH**

Lecturer

**ANOOP PRABHU**

Lecturer

**DARASHANA PUNGLIA**

Lecturer

**NATALIYA RAZUMILAVA**

Lecturer

**ANDREW READ**

Lecturer

**MICHAEL D. RICE**

Instructor

**MEGAN ELIZABETH RIEHL**

Instructor

**RAF S. RIZK**

Assistant Professor

**JOEL HOWARD RUBENSTEIN**

Associate Professor

**LIANGYOU RUI \***

Professor

**RICHARD J. SAAD**

Associate Professor

**SAMEER D. SAINI**

Assistant Professor

**LINDA C. SAMUELSON \***

Professor

**JAMES MICHAEL SCHEIMAN**

Professor

**PHILIP S. SCHOENFELD**

Adjunct Professor

**YATRIK M. SHAH \***

Associate Professor

**PRATIMA SHARMA**

Assistant Professor

**NEIL SHETH**

Lecturer

**DMITRY SHUSTER**

Lecturer

**ELIZABETH SPELIOTES**

Associate Professor

**JASON SPENCE**

Associate Professor

**RYAN WILLIAM STIDHAM**

Assistant Professor

**ELENA M. STOFFEL**

Assistant Professor

**GRACE L. SU**

Professor

\* Joint Appointment

**ANDREW W. TAI**  
Assistant Professor

**MIMI S. TAKAMI**  
Assistant Professor

**ELLIOTTAPPER**  
Assistant Professor

**ANDREA TODISCO**  
Professor

**STEPHANIE S. TSENG-ROGENSKI**  
Assistant Research Scientist

**DANIELLE KIM TURGEON**  
Professor

**MICHAEL VOLK**  
Adjunct Assistant Professor

**AKBAR WALJEE**  
Assistant Professor

**ERIK-JAN WAMSTEKER**  
Associate Professor

**THOMAS D. WANG**  
Professor

**JOHN W. WILEY**  
Professor

**JOHN ANDREW WILLIAMS \***  
Professor

**TADATAKA YAMADA**  
Adjunct Professor

**JUAN ZHOU**  
Research Investigator

**SHI-YI ZHOU**  
Assistant Research Scientist

**Instructional or Lecture Track**

Professor	16
Associate Professor	6
Assistant Professor	12
Clinical Lecturer	23
<b>Total:</b>	<b>57</b>

**Clinical Track**

Clinical Professor	2
Clinical Associate Professor	3
Clinical Assistant Professor	10
Clinical Instructor	3
<b>Total:</b>	<b>18</b>

Men	46 (61%)
Women	29 (39%)

**Research Track**

Assistant Research Scientist	9
Research Investigator	6
<b>Total:</b>	<b>15</b>

Luminal GI	60
Hepatology	15
<b>Subtotal:</b>	<b>75</b>

Research Track	15
Joint Appointment	9
<b>Total:</b>	<b>99</b>

## Endowed Professorships:

AN ENDURING LEGACY OF RESEARCH, CARE AND TRAINING

With the foresight and generosity of committed donors, the Division has established several endowed professorships. These chairs help to create an enduring legacy for the Division that enables and sustains our highly innovative research, patient care and training for the next generation of gastroenterologists.

### The H. Marvin Pollard Professorships

A nationally renowned pancreatic cancer researcher, Dr. Pollard was named head of the Section of Gastroenterology in 1940 and Chief of the Division of Gastroenterology in 1947. In 1956, Dr. Pollard secured funds to support Dr. Basil I. Hirschowitz' (Residency 1956) development of the first flexible fiberoptic gastroscope; Dr. Pollard helped develop and refine the device, the prototype of which is now housed in the Smithsonian.

Dr. Pollard retired in 1972. During his long and dedicated U-M career,

he touched the lives of thousands of patients with his skill and compassion. One of those patients was Shirley McLaughlin, who died in 1987 and whose husband Robert was grateful for the care his wife had received at U-M. Following Robert's death in 1989, his estate authorized the creation of two professorships at U-M, including the H. Marvin Pollard Professorship in Gastroenterology, established in 1993.

Two years later, a group of Dr. Pollard's former colleagues, friends and trainees joined forces to fund a second professorship bearing his name: the H. Marvin Pollard Collegiate Professorship in Gastroenterology. In

2006, distributions from the original fund created a third professorship: the H. Marvin Pollard Professorship in Internal Medicine. In 2008, further distributions funded the establishment of the H. Marvin Pollard Professorship in Gastrointestinal Sciences. In all, five professorships continue to honor Dr. Pollard's indelible legacy of leadership, research, teaching and healing.

### GRACE ELTA, MD H. Marvin Pollard Collegiate Professor of Gastroenterology

Dr. Grace Elta joined the Division faculty in 1982. She directs the Medical Procedures Unit and the Taubman Clinic



Grace Elta, MD, FASGE

Ambulatory Care Unit, and serves as Associate Chief of Clinical Programs. An experienced interventional endoscopist, Dr. Elta also heads the Pancreatic and Biliary Disorders Clinic, where she performs endoscopic ultrasound and therapeutic endoscopic retrograde cholangiopancreatography (ERCP).

The specialized ERCP procedure was first performed for diagnostic pur-

poses in the late 1970s at the U-M. In 1982, biliary sphincterotomy for stone extraction was added. The use of ERCP for treatment of pancreatic and biliary disorders has since grown tremendously and now includes pancreatic endotherapy and numerous biliary tract treatments. These procedures significantly reduce the need for invasive surgeries.

Dr. Elta's productive research program focuses on biliary tract disease, endoscopic ultrasound and pancreatic disease. She is a nationally renowned endoscopist who served as President of the American Society for Gastrointestinal Endoscopy (ASGE) in 2007 and the American Gastroenterological Association (AGA) DDW Council Chair beginning in 2013. She was inducted into the U-M Department of Internal

Medicine Clinical Excellence Society in 2013 and installed as H. Marvin Pollard Collegiate Professor of Gastroenterology in 2015.

**THOMAS D. WANG, MD, PhD**  
**H. Marvin Pollard Collegiate**  
**Professor of Endoscopy Research**

Dr. Thomas Wang joined the Division in 2007. The gifted physician scientist works at the forefront of molecular imaging, developing novel method-



Thomas D. Wang, MD PhD

ologies for *in vivo* imaging of the digestive tract for early cancer detection and staging.

Dr. Wang has developed confocal and multiphoton endomicroscopy platforms and the first video endoscope sensitive to fluorescence for rapidly identifying pre-malignant lesions over large mucosal surface areas. He has pioneered the use of fluorescence-labeled peptides to detect overexpressed cell surface targets *in vivo*.

Dr. Wang's approach—combining imaging information with biological markers—is addressing important clinical needs: the ability to differentiate lethal cancers from non-lethal disease, reducing overdiagnosis and lowering the number of false-positive and false-negative test results.

A popular teacher, Dr. Wang has mentored junior faculty, postdoctoral research fellows, clinical fellows, medical residents, medical students and many graduate and undergraduate students from U-M and around the world. He was installed as H. Marvin Pollard Collegiate Professor of Endoscopy Research in 2015.

**JUANITA L. MERCHANT, MD, PhD**  
**H. Marvin Pollard Professor of**  
**Gastrointestinal Sciences**

An internationally renowned molecular gastroenterologist, Dr. Juanita Merchant has made paradigm-shifting contributions to our understanding of the gastric response to chronic inflammation, including transcriptional control mechanisms in the GI tract.



Juanita Merchant, MD PhD

Dr. Merchant's laboratory demonstrated that gastrin is regulated by inflammatory mediators, leading to the reevaluation of *Helicobacter* pathogenesis and the control of acid secretion in the context of gastric inflammation. Her studies have led to the use of developmental paradigms in understanding how chronic inflammation alters the differentiation pattern of epithelial

cells in the stomach. Her laboratory also developed the first mouse model of gastric carcinoids. This *in vivo* model of a GI endocrine cancer will enable testing of new drug therapies.

As associate director of the U-M Medical Scientist (MD-PhD) Training Program, Dr. Merchant developed a clinical preceptorship for MSTP students and a pre-MSTP summer program for undergraduate students from groups currently underrepresented in science and medicine. Dr. Merchant's seminal research contributions were recognized by the American Gastroenterology Association (AGA) who awarded her the Distinguished Achievement Award in Basic Science (2017).

In recognition of her seminal work, Dr. Merchant was inducted into the

National Academy of Sciences Institute of Medicine in 2008. She was installed as H. Marvin Pollard Professor of Gastrointestinal Sciences in 2008.

**M. BISHR OMARY, MD, PhD**  
**H. Marvin Pollard Professor of Gastroenterology**

Professor and Chair, Department of Molecular & Integrative Physiology

M. Bishr Omary, MD, PhD, joined the Division in 2008 as H. Marvin Pollard



M. Bishr Omary, MD PhD

Professor of Gastroenterology and Chair of the University of Michigan Medical School Department of Molecular and Integrated Physiology. He has been an investigator at the VA Ann Arbor and Palo Alto Healthcare systems for 28 years.

Dr. Omary's research focuses on acute and chronic liver and pancreatic disorders as related to the intermediate filament cytoskeleton, genetic modifiers, porphyrias, biomarkers and therapeutic targets. Current work focuses on investigating intermediate filament proteins, termed keratin polypeptides 8, 18, 19 and 20 (K8/K18/K19/K20), which are specifically expressed in digestive-type epithelia. This includes studying their regulation through posttranslational modifications and associated proteins, defining

their function and disease pathophysiology, and using high throughput screening to identify compounds that may be used as potential therapy. This work is based on past findings from his laboratory that mutations in K8, K18 and K19 predispose their carriers to acute and chronic forms of liver disease and to disease progression.

Other current work involves studying the molecular pathogenesis and biologic significance of the hepatocyte inclusions called Mallory-Denk bodies. Dr. Omary's laboratory has identified several critical genetic and posttranslational modifications that are essential for inclusion formation. Additional ongoing studies are aimed at understanding the pathogenesis of porphyrias and why some patients with porphyria develop end-stage liver

disease. This includes the generation of zebrafish porphyria models and using these models to identify potential therapies.

Throughout his career, Dr. Omary has received many honors, named lectureships and mentorship awards. He trained many physician scientists and physiologists who have become leaders in their own right. In 2015 he received the AGA Distinguished Mentor Award. He served as the editor-in-chief of *Gastroenterology* from 2011 to 2016.

**CHUNG OWYANG, MD**  
**H. Marvin Pollard Professor of Internal Medicine**

Chung Owyang, MD is currently the H. Marvin Pollard Professor of Internal Medicine, Professor of Molecular and Integrative Physiology, Chief, Division



Chung Owyang, MD

of Gastroenterology and Hepatology and Director of the Pollard Institute for Medical Research at the University of Michigan Health System.

Dr. Owyang's own research interests have focused on the delineation of neurohormonal control of digestive functions including pancreatic endocrine and exocrine secretions, GI motility and eating behavior. Most recently,

his laboratory has focused on the role of microbiota in functional bowel diseases, intestinal inflammation and metabolic disorder. His research has provided important insights into the pathophysiology and treatment of human disease states particularly in the treatment of chronic pancreatitis and irritable bowel syndrome.

His laboratory characterized a new peptide, CCK-releasing factor, which is secreted into the intestinal lumen in response to food and stimulates CCK release. The pancreatic enzymes subsequently secreted into the lumen inactivate CCK-releasing factor, thereby creating a feedback regulatory loop. This novel observation has provided the basis for understanding the clinical utility of pancreatic enzyme supplements in alleviating pain in chronic

pancreatitis patients by diminishing CCK-mediated stimulation. Dr. Owyang also has a longstanding interest in the physiology and pathophysiology of gastrointestinal motility. Among his observations, using isolated cells, muscle strips and *in vivo* animal studies, he has demonstrated that somatostatin has both excitatory and inhibitory actions in myenteric cholinergic transmission and thus plays a critical role in mediating both limbs of the peristaltic reflex. He further demonstrated that in humans, somatostatin is a potent agent to initiate intestinal migrating motor complexes and thus can be effective in treating bowel bacterial overgrowth in patients with chronic intestinal pseudo-obstruction.

Dr. Owyang has received continuous NIH funding for more than 30 years,

and has published more than 300 original research and review articles. In recognition of his long and dedicated service to the University of Michigan, he received the Distinguished Service Award (2010) and the Paul De Kruif Lifetime Achievement Award (2016).

At the national level, Dr. Owyang was honored by the American Gastroenterological Association (AGA) with the Distinguished Mentor Award (2011), which recognizes an individual for his/her achievement as an outstanding mentor over a lifelong career. In 2013, he received the AGA Julius Friedenwald Medal, the highest honor the AGA bestows on a member.

Throughout his career Dr. Owyang has actively promoted research and educational training at the international level and has trained many

gastroenterologists who now hold leadership positions in their home countries. In recognition of this work, he was awarded a Royal College of Physicians (Thailand) Honorary Fellowship and has been given Honorary Professorships by more than 10 top universities in China.

**WILLIAM D. CHEY, MD**  
**Timothy T. Nostrant Collegiate Professor in Gastroenterology**

Dr. Timothy Nostrant joined the U-M Department of Medicine as a House Officer in 1973 and completed his residency and Gastroenterology Fellowship at U-M in 1979. He soon joined the faculty and, over the next 36 years, emerged as an outstanding diagnostician, a motivating teacher and a visionary leader. In 1981-83, Dr. Nostrant served as interim Chief of

the Division of Gastroenterology and Hepatology.

Dr. Nostrant developed the infrastructure for the Division's clinical operations. In the early 1980s, he formalized clinical procedures and systems, many still in place today. He also recognized the increasingly important role endoscopy would play as a major diagnostic tool in the field of gastroenterology and was integral to the creation of the highly successful Medical Procedures Unit (MPU) at U-M.

Widely respected for his clinical knowledge and passion for education, Dr. Nostrant earned numerous awards for his teaching contributions. He trained over 300 fellows, including many of the Division's key clinical faculty members. He also led the Faculty Diagnostic Unit, a productive consul-

tative service within the Department of Internal Medicine that served as a national model for the development of the Clinician Scholar track.

Dr. Nostrant's many contributions to the Division and to the field of gastroenterology are honored in perpetuity with the Timothy T. Nostrant Collegiate Professorship in Gastroenterology, established by Dr. Nostrant's family and colleagues in 2010.

Today, **WILLIAM D. CHEY, MD**, holds the Timothy T. Nostrant Collegiate Professorship. Dr. Chey (Fellowship 1993) directs the GI Physiology Laboratory and co-directs the Michigan Bowel Control Program. He also runs an active clinical research group, which has received funding from both federal and private sources. He has authored more than 200 man-



William D. Chey, MD

uscripts, reviews and book chapters and served as co-editor-in-chief of the *American Journal of Gastroenterology* from 2010 to 2016. He also serves on the editorial boards of several other journals.

Dr. Chey has participated in and directed numerous national and international continuing medical education programs in gastroenterology, and

has been elected to the roster of "Best Doctors" since 2001 and "America's Top Doctors" since 2009. In 2010, he was named one of the "75 Best Gastroenterologists in America" by Becker's ASC Review.

**ANNA S.F. LOK, MD, FRCP**  
**Alice Lohrman Andrews Research Professor of Hepatology**

The Alice Lohrman Andrews Research Professorship in Hepatology was established by Charles J. "Chuck" and Judy Andrews. The professorship is named for Chuck's late wife, Alice Lohrman Andrews, who died in 1996 from complications of liver disease.

A native of Detroit and graduate of Redford High School, Alice Lohrman earned her bachelor's degree in education from the University of

Michigan in 1960. She met Chuck in 1958 at a social mixer, and they were married in 1961. A fellow U-M alum, with a degree in business, Chuck rose through the executive ranks at Ford Motor Company. Alice taught school, taking a particular interest in children with special needs; in later years, she sold real estate. She was also active as a national officer in her sorority, Alpha Chi Omega. The couple, who shared a love of U-M football and basketball, raised three children.

In the mid-1990s, Alice was diagnosed with liver disease. The family sought care from world-renowned hepatologist **ANNA LOK, MD**. When Alice lost her life to the disease in 1996, the family philanthropic organization TUKTAWA (pronounced "tucked away") was directed to make gifts to support Dr.



Anna Lok, MD

Lok's research toward more effective treatments and, eventually, a cure.

In December 2007, the foundation decided to further support Dr. Lok's work by establishing a professorship in Alice's name in order to advance the world-class research in liver disease at U-M, made possible by Dr. Lok's leadership of the hepatology team in the Division.

Dr. Lok continues to hold the Alice Lohrman Andrews Research Professorship in Hepatology today, and her work is transforming how diseases of the liver are diagnosed, managed and treated. Her research focuses on the natural history and treatment of hepatitis B and C, and the prevention of liver cancer. She has published more than 350 papers on viral hepatitis and liver diseases and is the coauthor of the American Association for the Study of Liver Diseases (AASLD) Practice *Guidelines on Hepatitis B*, a reference for physicians all over the world.

In a landmark study of hepatitis C, published in 2012, Dr. Lok and colleagues showed it was possible to achieve a sustained virologic response in patients infected with genotype 1 of the virus using a combination of

all-oral, direct-acting antiviral agents (DAAs), rather than the standard therapy of ribavirin and interferon (*New England Journal of Medicine*, 2012; 366:216-224). She is now investigating different combinations of DAAs that might further shorten treatment and improve cure rates for additional virus genotypes as well as among patients with advanced liver disease and those who have failed prior treatment.

Dr. Lok has received many awards for her work, including the Distinguished Scientist Award from the Hepatitis B Foundation in 2008, the Distinguished Women Scientist Award from the American Gastroenterological Association (AGA) in 2008, the Distinguished Service Award from the AASLD in 2011, the AGA's William Beaumont Prize in 2016,

and was inducted into the Department of Internal Medicine Clinical Excellence in 2013. She has been included in the list of "Best Doctors" and "Who's Who" for many years and will be president of AASLD beginning January 1, 2017.

#### **The Chung Owyang, MD, Professorship in Gastroenterology**

Chung Owyang, MD, has established an international reputation as a leader in gastroenterology over his more than quarter-century as Chief of the University of Michigan Division of Gastroenterology and Hepatology. He is the longest-serving GI division chief in the country.

Dr. Owyang has overseen the Division's growth from a dozen faculty members in 1990 to more than 80 today, in ad-

dition to 23 fellows and more than 250 staff. Under his leadership, the Division established the University of Michigan Center for Gastrointestinal Research, the first of its kind in the nation. The Division is one of the most highly recognized groups of gastroenterologists in the world, noted for innovation, excellence and leadership in emerging areas of basic, translational and clinical research and in clinical care.

To commemorate Dr. Owyang's career, Dr. John Carethers, Chair of the Department of Internal Medicine and the Division have established the Chung Owyang, MD, Professorship in Gastroenterology. This chair will support future chiefs of the Division of Gastroenterology and Hepatology. The Chung Owyang, MD, Professorship in Gastroenterology will ensure that Dr.

Owyang's legacy of selfless dedication will live on at the University of Michigan in perpetuity.

#### **The Keith S. Henley, MD, Collegiate Professorship in Gastroenterology**

From 1954—when he joined the University of Michigan Medical School faculty—until his death in 2010, Keith S. Henley, MD, dedicated himself to his research, clinical and teaching duties in the Division of Gastroenterology and Hepatology. Today, physicians and researchers across the country cite Dr. Henley as one of their most valued mentors.

Dr. Henley was named professor of internal medicine in 1968. He took over leadership of the Division of Gastroenterology as chief in 1972

and founded the U-M Hepatology Program that same year, bringing together a highly talented group of hepatologists. He led the Division as chief until 1981 and retired in 1993, although he continued to serve the U-M Medical School in many ways.

A world-renowned hepatologist, Dr. Henley's primary research focus during the latter part of his career and into retirement was the development of an infrastructure to aid in the education and care of hepatitis patients in Vietnam and other countries afflicted with high incidences of the disease.

In 2007, Dr. Henley's colleagues began work to endow the Keith S. Henley, MD, Collegiate Professorship in Gastroenterology. Dr. Henley and his family contributed generously to the fund, as did many colleagues,

former trainees and the Department of Internal Medicine. Dr. Henley found the professorship, established in 2008, deeply meaningful.

**JOSEPH KOLARS, MD**  
**Josiah Macy, Jr. Professorship in Health Professions Education**

After Kate Macy Ladd's father died of yellow fever in 1876 when he was just 38, she was moved to establish a medical research foundation in his honor. The Josiah Macy Jr. Foundation supports programs designed to improve the education of physicians and enhance the representation of minorities in the healthcare profession.

Ladd's dedicated financial support enabled the foundation to award grants that advanced research in such areas as traumatic shock and war-related psychiatric disorders, aging and arteriosclero-

sis, genetics and human development and psychosomatic medicine. In 1996, the New York City-based philanthropic foundation selected the University of Michigan Medical School (UMMS) from among 51 competing applicants for the grant that funded this professorship.

Today, **JOSEPH KOLARS, MD** (Fellowship 1989), holds the Josiah Macy, Jr. Professorship in Health Professions Education. Dr. Kolars



Joseph Kolars, MD

became UMMS' first senior associate dean for education and global initiatives in 2009. In that role, he serves as UMMS lead for the oversight and expansion of the education mission and global initiatives.

Dr. Kolars' career has been focused on physician education, and he has held a number of leadership roles in education programs for medical students, residents and fellows, including program director of one of the largest internal medicine residencies in the United States. His scholarship has largely emphasized educational outcomes, measurements of competency, faculty development and effective learning venues.

Dr. Kolars has extensive international experience, including numerous faculty development programs worldwide. In 2010, he was appointed inaugural

co-director of the Joint Institute for Clinical and Translational Research between the University of Michigan Medical School and Peking University Health Science Center. The Joint Institute facilitates collaborative research projects and training initiatives between the schools and their affiliated hospitals.

He has given lectures and/or conducted classes in many parts of the world, including China, Malaysia, Thailand, India, Peru, Germany, Pakistan, South Africa, Ghana, Uganda, Tanzania and Vietnam. For more than three years, he lived in Shanghai with his family to establish a new healthcare system that could also serve as a learning site for local physicians. He has also worked with the Bill and Melinda Gates Foundation on education systems that will build human resource capacity to transform health.

## Established Lectureships

The Division of Gastroenterology and Hepatology and the Department of Internal Medicine have established four lectureships to honor individuals who have made significant contributions to clinical care, teaching and research. Each Lectureship is used to bring a leading expert to the University of Michigan to present a lecture.

**Tadataka "Tachi" Yamada, MD, KBE Lectureship** – world leaders in gastrointestinal investigation

In 1983, Dr. Tadataka (Tachi) Yamada was recruited by Dr. William Kelley to join the University of Michigan as Professor of Internal Medicine and Chief of Gastroenterology. Tachi approached his new position with great enthusiasm and fervor. Under his leadership, the Division became the premier division in the country. The Digestive Disease Center, funded by the NIH with Dr. Yamada as the PI was critical to the development of the Michigan Gastrointestinal Peptide Research Center, the first NIH Peptide Research Center in the country.

Today, this center is in its 30 year of continuous funding from the NIH. Dr. Yamada's exceptional success as a Division Chief led to his appointment as the John G. Searle Professor and Chair of the Department of Internal Medicine in 1990. In February 1996, he was named as the President of the Healthcare Division and Executive Director of SmithKline Beecham. Subsequently, he became Chair of Research and Development for GlaxoSmithKline. In 2005, Bill Gates selected Dr. Yamada to run the Bill and Melinda Gates Foundation Global Health Program. Under his leadership, the Gates Foundation engaged in the clinical development of 70 vaccine and

new pharmaceutical entities which promise relief from suffering for the poorest people of the world.

For his significant contributions, Dr. Yamada received an honorary appointment as Knight Commander of the Most Excellent Order of the British Empire (KBE). He was also a member of the President's Council of Advisors on Science and Technology.

Dr. Yamada remains actively involved in academics as Adjunct Professor at the University of Michigan, maintaining a tie with his roots to serve as a bridge between academia, industry and philanthropy. In many ways, Tachi Yamada exemplifies how

a physician can continue to grow and develop through myriad careers to provide care and service to patients wherever they may be.

The Division of Gastroenterology and Hepatology developed this lectureship to honor Dr. Yamada. Each year a world-renowned leader in Gastrointestinal Sciences is invited to present the Yamada Lecture.

**Timothy T. Nostrant, MD Lectureship in Gastroenterology** – national leaders in education

Dr. Nostrant came to the University of Michigan as a house officer in 1973. He completed a fellowship in gastroenterology in 1979 and then became a faculty member. Throughout his career, he exhibited the attributes of a master clinician: trusted by his patients, respected by his colleagues

and admired by his students. He was an outstanding diagnostician, skillful endoscopist and compassionate teacher. His tremendous clinical knowledge and judgment made him the "go-to" person in the Division of Gastroenterology and Hepatology and one of the most popular gastroenterologists in Michigan.

Dr. Nostrant had a strong passion for medical education. Whether in the ward or classroom, he selflessly provided consultation and teaching to students, fellows and junior faculty members. He trained more than 300 fellows who are now practicing in 33 states. Dr. Nostrant received numerous awards for his teaching contributions, including the Outstanding Clinician Award from the Office of the Dean in 2008, AGA Distinguished Clinician Award

and was a charter member of the Department of Internal Medicine Clinical Excellence Society.

To honor Dr. Nostrant, the Division established the Timothy T. Nostrant Lectureship in Gastroenterology. Each year a world leader in clinical gastroenterology is invited to present the Nostrant Lecture.

**Dame Sheila Sherlock MD Visiting Lectureship in Hepatology** - world leaders in hepatology

In 1959, Dr. Sheila Sherlock was appointed to the Chair of the Department of Medicine at the Royal Free Hospital School of Medicine. She was the first woman to be appointed to the Chair of Medicine in a British medical school. Dr. Sherlock's unit

at the Royal Free was the "Mecca of Hepatology" for referring physicians worldwide and THE Liver Center for trainees in Hepatology from the 1960s to the 1980s. Dr. Sherlock published more than 600 papers, and wrote or edited over 25 books. She trained more than 300 physicians and investigators, many of whom went on to be directors of liver units all over the world. She remained very close to all her trainees and considered every one as part of the "Sherlock Family". In 1978, Dr. Sherlock was knighted by the Queen of England as "Dame Commander of the British Empire" for her contributions to medicine.

Education and training of other physicians in liver diseases has been a cornerstone of Dr. Sherlock's work. Keith Henley, MD, the first

hepatologist at the University of Michigan and Anna Lok, MD, who has been Director of Clinical Hepatology at the University of Michigan since 1995 both received their training in hepatology under the tutelage of Dame Sheila Sherlock.

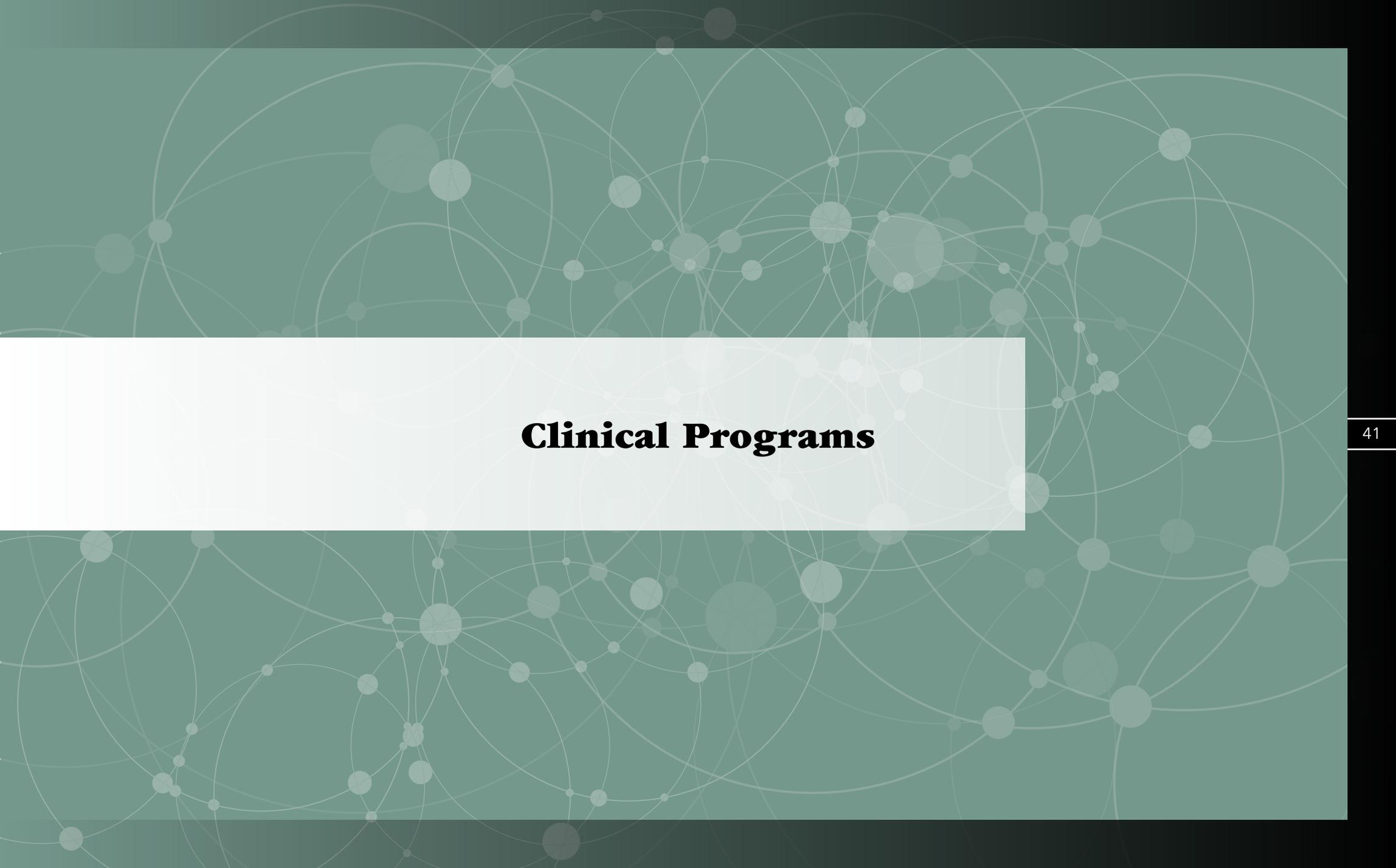
To honor her mentor, Dr. Anna Lok and the Divisions of Gastroenterology and Hepatology established this lectureship.

Each year a world leader in hepatology will be invited to present the Dame Sheila Sherlock, MD Lecture on an important topic in liver disorders.

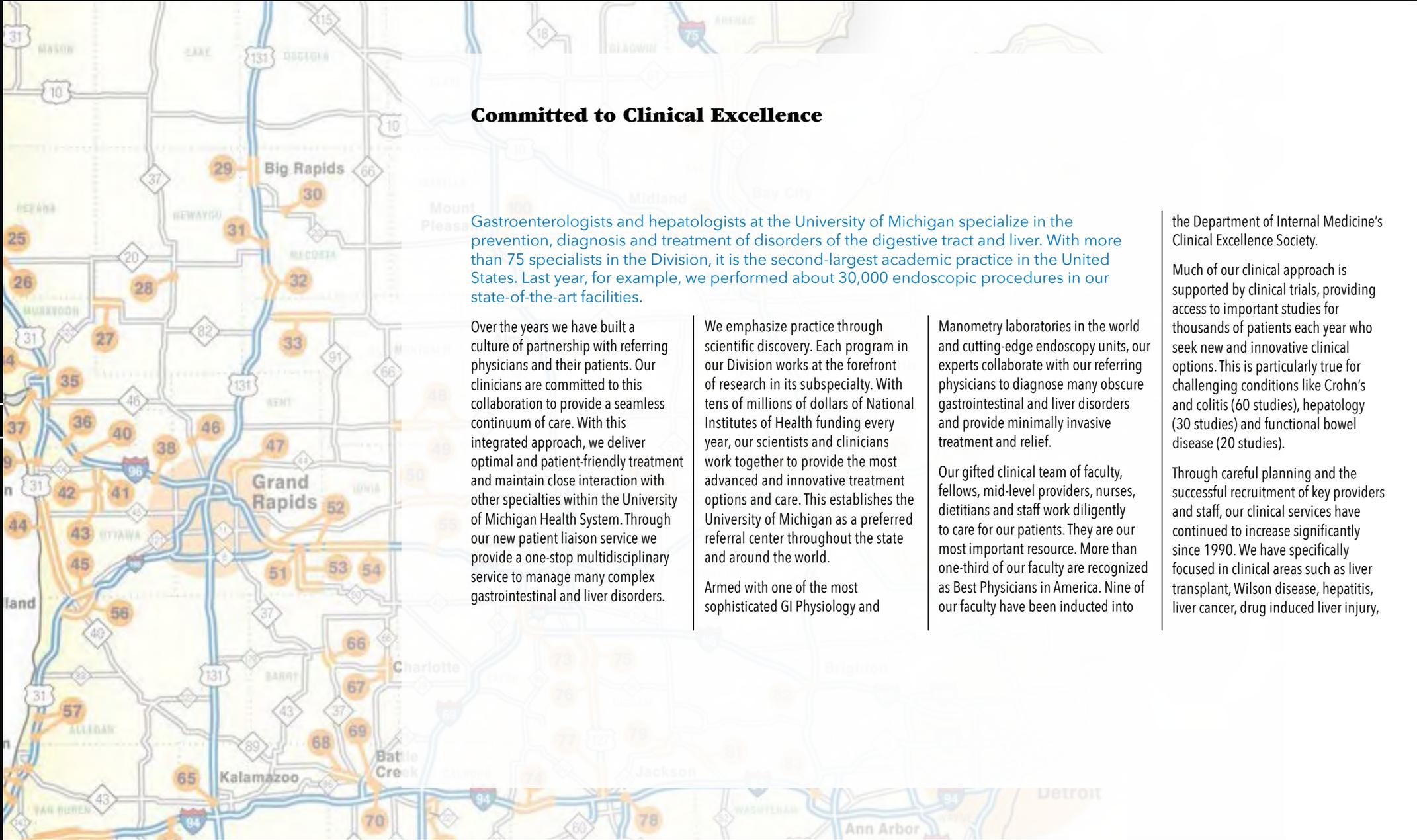
**Terry M. Logan, RN Gastroenterology Nurse Education Fund**

- national leaders to support nursing education

For 20 years, Terry served at the University of Michigan in several capacities, most notably in the GI outpatient clinic. Terry was well known for her diligence, compassion, exemplary service and commitment to nursing. This fund serves to establish within the Division a legacy of excellence in nursing care and to support visits to U-M by key leaders who will share the latest advancements in patient care, clinical research and technology in nursing.



# **Clinical Programs**



## Committed to Clinical Excellence

Gastroenterologists and hepatologists at the University of Michigan specialize in the prevention, diagnosis and treatment of disorders of the digestive tract and liver. With more than 75 specialists in the Division, it is the second-largest academic practice in the United States. Last year, for example, we performed about 30,000 endoscopic procedures in our state-of-the-art facilities.

Over the years we have built a culture of partnership with referring physicians and their patients. Our clinicians are committed to this collaboration to provide a seamless continuum of care. With this integrated approach, we deliver optimal and patient-friendly treatment and maintain close interaction with other specialties within the University of Michigan Health System. Through our new patient liaison service we provide a one-stop multidisciplinary service to manage many complex gastrointestinal and liver disorders.

We emphasize practice through scientific discovery. Each program in our Division works at the forefront of research in its subspecialty. With tens of millions of dollars of National Institutes of Health funding every year, our scientists and clinicians work together to provide the most advanced and innovative treatment options and care. This establishes the University of Michigan as a preferred referral center throughout the state and around the world.

Armed with one of the most sophisticated GI Physiology and

Manometry laboratories in the world and cutting-edge endoscopy units, our experts collaborate with our referring physicians to diagnose many obscure gastrointestinal and liver disorders and provide minimally invasive treatment and relief.

Our gifted clinical team of faculty, fellows, mid-level providers, nurses, dietitians and staff work diligently to care for our patients. They are our most important resource. More than one-third of our faculty are recognized as Best Physicians in America. Nine of our faculty have been inducted into

the Department of Internal Medicine's Clinical Excellence Society.

Much of our clinical approach is supported by clinical trials, providing access to important studies for thousands of patients each year who seek new and innovative clinical options. This is particularly true for challenging conditions like Crohn's and colitis (60 studies), hepatology (30 studies) and functional bowel disease (20 studies).

Through careful planning and the successful recruitment of key providers and staff, our clinical services have continued to increase significantly since 1990. We have specifically focused in clinical areas such as liver transplant, Wilson disease, hepatitis, liver cancer, drug induced liver injury,

## CLINICAL PROGRAMS

Crohn's and colitis, functional bowel disease, pancreas and biliary system, small bowel and general GI. We have determined that these challenging areas are best served by developing focused, multidisciplinary teams. The number of clinic locations has increased from one each at the U-M and VA to 16 clinics.

**UH Taubman** – GI all programs

**UH Taubman** – Hepatology and Transplant

**Cancer Center** – Liver Cancer

**Cancer Center** – Cancer Genetics

**Women's and Children's** – Michigan Bowel Control

**Briarwood** – General GI, IBS

**Brighton** – IBD, Hepatology, IBS, General

**Canton** – Hepatology, General GI, Esophageal

**Dexter** – General, IBS

**East Ann Arbor** – General GI, IBD, Geriatric GI

**Grand Rapids** – Advanced Hepatology

**Livonia** – General, Pancreatic Biliary

**Northville** – All programs

**Saline** – General GI, IBD

**VA** – GI Lumen

**VA** – Hepatology

Over this same period of time, clinic visits increased 255 percent, from 11,693 in FY1991 to 41,532 in FY2016.

Endoscopic programs have similarly developed in focused areas of the

esophagus (EMR, banding, dilation), stomach, interventional endoscopy (EMR, ERCP, EUS, POEM), Crohn's and colitis and small bowel (capsule endoscopy, double balloon enteroscopy). Facilities have increased from one each at U-M and VA to five (UH, VA, East, Livonia, Northville), supporting a 472 percent increase in procedures, from 5,518 in FY1991 to over 30,000 in FY2016.

Our GI Physiology program has grown dramatically as we are better able to measure and quantify the impact of electrical signals and pathways, acidity and muscle contractions. While providing only a few hundred diagnostic tests in FY1991, our GI Physiology Laboratory now provides over 7,000 tests each year.



To better meet the needs of our patients, we are continuing to expand to new locations throughout the region as well as within Ann Arbor:

**West Ann Arbor** (FY18)  
Primary and Subspecialty Clinics

**Brighton Health Center** (FY19)  
Endoscopy, ORs, Clinics

**East Ann Arbor Phase II** (FY22)  
Endoscopy, ORs, Clinics

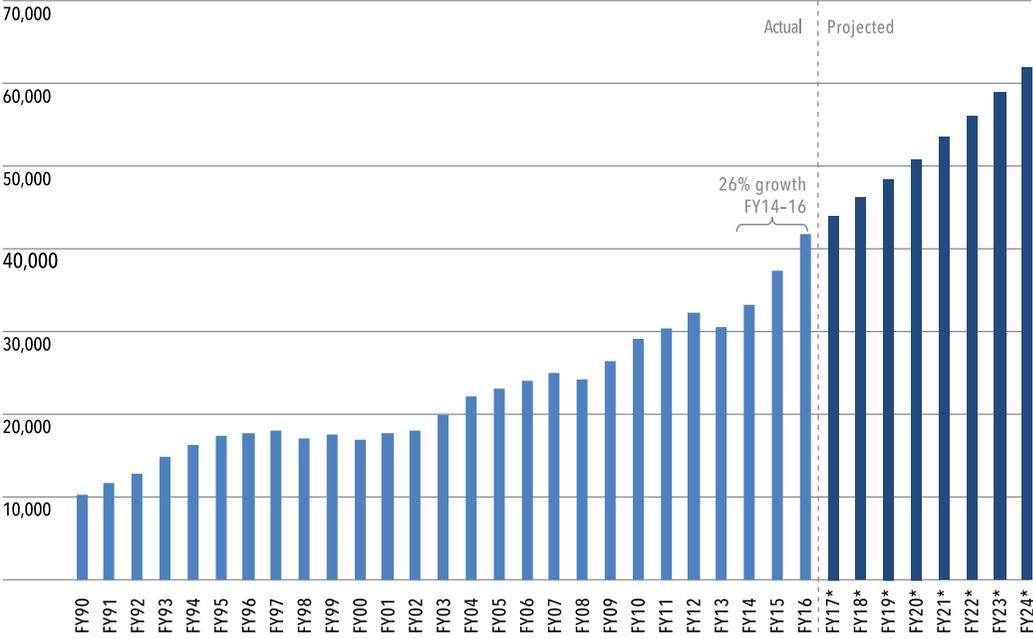
**New 230 Bed Patient Tower** (FY23)  
120 incremental beds

**Northville II** (FY24)  
ORs, Clinics

To meet the Medical Center's plan for expansion, we expect to recruit many additional faculty and staff.

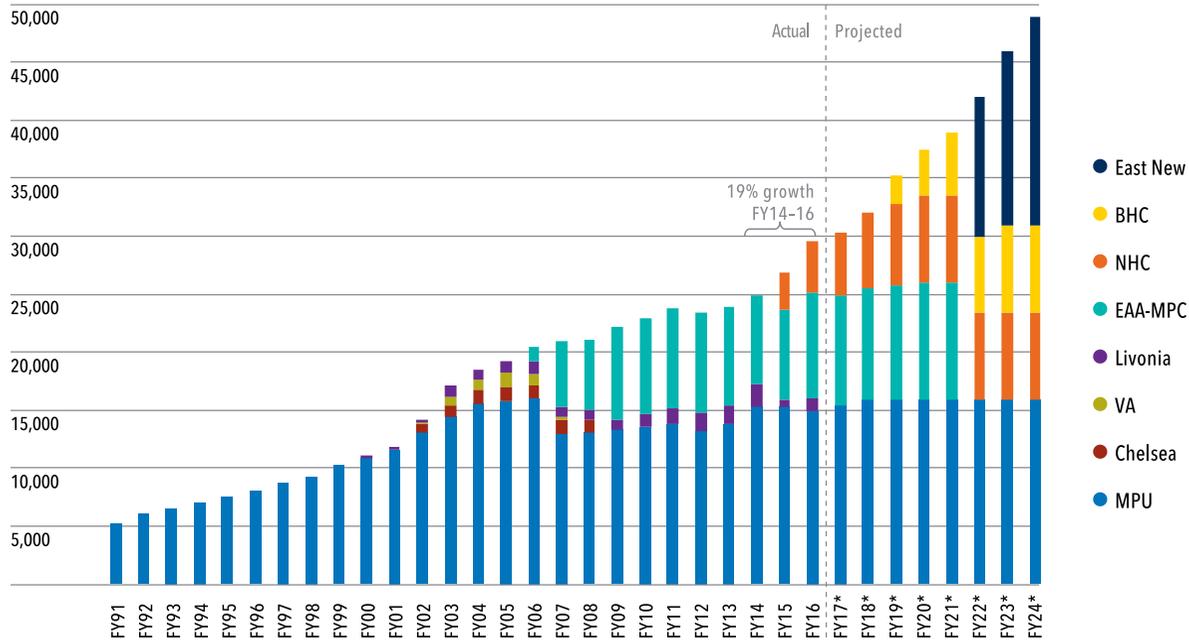
Growth projections for clinic and endoscopy activity are shown in the following charts.

**GI Clinic Visits**



\*Projections include MPU, EAA-MPC and NHC at full capacity by FY20. Growth beyond that is from BHC and EAA-MPC replacement (East New)

## GI Endoscopy



\*Projections include MPU, EAA-MPC and NHC at full capacity by FY20. Growth beyond that is from BHC and EAA-MPC replacement (East New)

With our robust infrastructure, world-class faculty and a firm commitment to serve, we offer patients the most advanced, safest and proven medical treatments for gastrointestinal and liver disorders. This is the Michigan Difference!

## GI Leadership Lays Foundation for Clinical Research

A significant milestone in the history of the Division of Gastroenterology was the establishment in the late 1960s of the Clinical Research Unit (CRU). Headed by **ARTHUR FRENCH, MD**, the CRU was one of only six such entities in the country supported by the National Institutes of Health to provide much-needed infrastructure for clinical investigations.

Dr. French's own research focused on malabsorption. In collaboration with **ROBERT J. BOLT, MD**, he developed the multiple-retrieving small bowel biopsy tube, which enabled them to perform the first intestinal biopsy and to make the association between flattened villi and malabsorption in celiac disease.

In the 1970s, the CRU transitioned to the NIH General Clinical Research Center (GCRC) model. It played a pivotal role in supporting numerous studies focusing on the GI tract including:

- a collaboration between **PAUL WATKINS, MD**, **JOSEPH KOLARS, MD**, and **ROBERT FONTANA, MD** in the Division of Gastroenterology that established an important role for the gut lumen-based cytochrome p450 enzymes in drug metabolism and modulation of this pathway by specific foods including grapefruit
- the collaboration between **GEORGE BREWER, MD**, in the Division of Human Genetics, and **FRED ASKARI, MD, PhD**, in the Division of Gastroenterology, demonstrating that oral zinc is an effective therapy for Wilson disease. Treatment with zinc acetate remains the standard of care for Wilson disease today;
- a collaboration between **HARI CONJEEVARAM, MD, MSc**, in the Division of Gastroenterology and **CHUCK BURANT, MD, PhD**, in the Division of Endocrinology and Metabolism, examining the pathophysiology of non-alcoholic fatty liver disease.

Over the years the Division's faculty have provided strong leadership of the GCRC. **DR. WATKINS**, a renowned

expert in drug-induced liver disease, led the Center in the 1990s. **JOHN W. WILEY, MD**, an expert in neurophysiology and the brain-gut axis, served as director from 1999 to 2012. During his tenure, the GCRC was funded by the largest NIH grant based at the University of Michigan medical campus at that time.

Dr. Wiley also served as president of the GRCR Program Directors Association. During his tenure, he helped guide the transition of the GCRC model to the current model, supported by the NIH Clinical Translational Sciences Award (CTSA) program. This innovative model allows more flexible allocation of resources to support clinical research at the institutional level. Today, the CTSA grant at the University of Michigan serves as the clinical research hub

for more than 170 departments and divisions; it also collaborates through a nationwide consortium to advance clinical and translational discoveries that improve care of patients.



Arthur French, MD

**Rare Care:**  
**MULTIDISCIPLINARY CLINIC FOR PATIENTS WITH WILSON DISEASE**

A rare, hereditary metabolic liver disorder that impedes the cellular transport of copper, Wilson disease affects about 6,000 individuals in the United States. Delays in diagnosis are common. But as copper collects in liver, brain and other tissues, the disease can cause a range of dangerous symptoms easily mistaken for those of many neurologic and psychiatric disorders.

"Many doctors might only see one or two patients with Wilson disease in their career," said **FRED ASKARI, MD, PhD**, director of the University of Michigan Wilson Disease Center of Excellence. "In contrast, we see hundreds, and we learn more from every one."

The U-M has a history of successful management and treatment of Wilson disease dating back to the 1990s, when—in the course of conducting research on sickle cell anemia—a team of physicians led by **DR. GEORGE BREWER** discovered that zinc caused copper

deficiency and applied the findings to Wilson disease. His team's work was instrumental in translating a scientific discovery into an FDA-approved therapy with zinc acetate, which has since been adopted worldwide.

Treatment at U-M also includes highly multidisciplinary care. Patients may be seen by adult or pediatric hepatologists, neurologists, speech pathologists, liver transplant specialists, dietitians, genetic counselors and psychiatrists. The Center's laboratory technicians specialize in urinary copper quantitation, and a nurse

specialist and patient coordinator have extensive experience working with families affected by Wilson disease.

In addition to treating patients and conducting ongoing research, Dr. Askari and colleagues teach U-M medical students, residents and Gastroenterology and Liver Transplant fellows about the disease and consult with physicians globally. Efforts are underway to establish international care networks and telemedicine programs to further develop physician expertise and reduce the need for patients to travel long distances.

"Wilson disease presents clinicians with many questions and special situations that vary from patient to patient. That's part of the challenge and why it's so important to learn how to recognize and diagnose it," said Dr. Askari. "There's nothing more gratifying to me than for a colleague to call me up and say, 'Hey, I diagnosed a case of Wilson disease.'"



Fred Askari, MD, PhD

DRUG INDUCED LIVER INJURY, ACUTE LIVER FAILURE, WILSON DISEASE, CIRRHOSIS CARE

VIRAL HEPATITIS

LIVER CANCER

FATTY LIVER/NAFLD

LIVER TRANSPLANTATION

## Clinical Hepatology:

PROVIDING CUTTING-EDGE, COMPASSIONATE, MULTIDISCIPLINARY CARE FOR LIVER DISEASE

With 15 faculty and close to 12,000 patient visits annually, the Hepatology Program at the University of Michigan Health System is one of the largest in the nation. One of the oldest clinical hepatology programs, it offers expertise in a wide range of liver diseases, including drug-induced liver injury, acute liver failure, cirrhosis, fatty liver/NAFLD, viral hepatitis and liver cancer. Since its start in the 1970s, the program has achieved national and international recognition.

Initially housed at the main University Hospital campus, the Hepatology Program now has clinics in Brighton, Canton, Northville and, monthly, in Grand Rapids, with other prospective Michigan locations under consideration.

"Over time, you can't stay in one place; rather than ask patients to come to us, we are going

out to patients and providing care in many areas," noted **ANNA LOK, MD, FRCP**, Director of Clinical Hepatology.

### Focused clinics offer specialized care

The Hepatology Program has also developed three highly sought, multidisciplinary clinics in Liver Transplant, Liver Tumor and Wilson Disease. Through the Liver Transplant Clinic, established 21 years ago, patients have access to hepatologists, transplant surgeons, social workers, psychiatrists and dietitians in one visit.

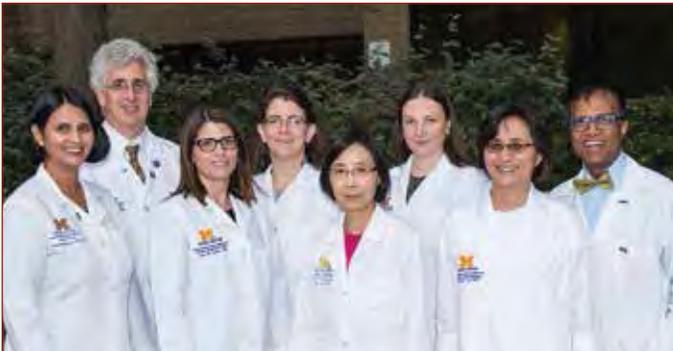
Similarly, through the Liver Tumor Clinic, patient care is coordinated among surgeons, oncologists, hepatologists and radiologists. A longstanding Liver Tumor Board now offers referring physicians an opportunity to participate virtually in meetings to discuss treatment options, allowing some patients to get consultative care without having to travel. The Hepatology Program runs a second Liver Tumor Clinic and Tumor Board at the VA Ann Arbor Healthcare System.

Staffed by a multidisciplinary care team, the Wilson Disease Center of Excellence

runs a monthly Wilson Disease Clinic. Based on individual need, patients can see speech pathologists, neurologists, dietitians, genetic counselors and psychiatrists in one visit. Laboratory technicians supporting the Center are specially trained in the quantification of copper, and a nurse specialist and patient coordinator focus on the unique needs of individuals and families affected by this rare disease.

### Training hepatologists worldwide

The Division's three-year Gastroenterology Fellowship includes training in all aspects of hepatology. In addition, the Division offers a fourth-year Transplant Hepatology Fellowship. More than a dozen fellows have graduated from this program, and many are now faculty in other academic hepatology programs.



Dr. Lok herself has trained over 20 fellows from all parts of the globe since she joined the University of Michigan faculty in 1995. Several of these fellows are now full professors, and some are chiefs of medicine or gastroenterology divisions.

### Leadership in clinical research

With a broad research portfolio, the Hepatology Program's investigations span scientific, clinical and health services research. Research efforts are funded by the National Institutes of Health (R01, U01, K08, R03), U.S. Department of Veterans Affairs, American Association for the Study of Liver Diseases, American Gastroenterological Association and the Doris Duke Charitable Foundation, as well as philanthropic, industry and

U-M sources. Several faculty head large, multi-center, clinical research networks funded by the National Institutes of Health, including those focused on acute liver failure, drug-induced liver injury, hepatitis B and biomarkers for early diagnosis of hepatocellular carcinoma. Faculty across the Hepatology Program publish an average of 64 articles in peer-reviewed journals annually.

Groundbreaking research into hepatitis C is leading to new all-oral drug regimens, with significantly reduced side effects and improved cure rates for patients. Other faculty have made pioneering discoveries of genetic markers associated with obesity and fatty liver. Yet others have provided valuable data on liver organ allocation, leading to changes in national policies.

"Our physicians and physician-scientists have emerged as leaders at the national level," Dr. Lok said. "As a result, our patients benefit by having access to experimental therapies and effective new treatment approaches. The new insights and knowledge generated by our faculty benefit not just our patients but also patients worldwide. The large number of former fellows in practice in more than 10 states in the United States and in 10 countries magnify the impact of the Michigan Hepatology Program on our field and on patients with liver diseases around the world."



Anna Lok, MD, FRCP

**Claudia Dionne**  
HEARING THE WORD "CURE"

**For Claudia Dionne, it's hard to remember life before what she calls "the discovery": the devastating news that she had viral hepatitis.**

"I just knew my life had changed forever," she said. "I went for my yearly checkup like I had done forever and ever and ever—and lo and behold, I was at dinner that night when my doctor called and broke the news: I had hepatitis C."

Hepatitis C affects some three to four million Americans, causing inflammation and damage to the liver. For the past few years, the only treatment has been a grueling combination of injectable medicines,

often with serious side effects. Perhaps even more frustrating has been the low cure rate: typically only 40 to 50 percent of patients clear the virus.

But hepatologists at the University of Michigan, including Dr. Anna Lok, led the first clinical trial that proved that a combination of oral drugs can eradicate hepatitis C even in the most difficult cases. The discovery allows patients like Claudia to clear the virus, preventing the threat of liver failure and liver cancer.

The findings from that first study were published in the *New England Journal of Medicine* (2012; 366:216-224) and paved the way for testing and approval of other combinations of direct-acting antiviral agents for hepatitis C.

"Claudia was one of the first patients in the world to be cured with a combination of oral pills," said Dr. Lok. "She was declared cured in early 2012, two years before any of the combinations of oral pills were approved. This is a benefit of participating in clinical trials, although not all trials lead to positive results and some carry risks. As researchers, we are forever grateful to patients who put their faith in us and undertake risks that benefit science and other patients with the same disease."

In the past three years, 10 direct-acting antiviral agents have been approved for use in various combinations, and the vast majority of patients can expect a 90 to 95 percent cure rate after only 12 weeks of pills. "Treatment now is highly effective and

simple, with minimal side effects," said Dr. Lok. "The current challenge is to make sure patients are diagnosed and referred early."

Claudia was skeptical at first, wavering between hope and disbelief. "A couple of pills a day and that's it?" she wondered. It seemed too easy. And then she heard the word from Dr. Lok she wasn't sure she would ever hear. "Dr. Lok never used that word with me, until one day she looked at me and said, 'You're cured.'"

Because Claudia was diagnosed early, she will not need to worry about cirrhosis or liver cancer in the future. In fact, she has been discharged from the liver clinic or, in Dr. Lok's words, "Claudia has graduated from my care."

## Patient Story



## The History of Liver Transplant

The University of Michigan Liver Transplant Program was one of the first 10 such programs established in the United States. The first transplant done on August 2, 1985 required a team of more than 50 staff including surgeons, nurses, perfusionists and myriad support staff. Over time, the duration of the operation, the need for blood products and other aspects of medical and surgical innovation led to a tremendous expansion of this intervention from a little over 400 transplants nationally per year in the early 1980s to nearly 7,500 per year in 2016. Milestones in the University of Michigan program include seminal studies by Drs. Henley and Lucey describing successful outcomes in patients with alcoholic cirrhosis, hepatitis B infection and liver cancer. In 2002, Dr. Fontana

was appointed medical director; additional innovations since that time have included the utilization of living donor transplantation, use of deceased cardiac donors, testing of extracorporeal liver support devices and major improvements in the control of hepatitis B and C both pre- and post-transplant. Throughout the history of the program, success has required the input of a

large number of dedicated individuals including nurses, mid-level providers, GI fellows, therapeutic endoscopists and a cadre of collaborators in pathology, radiology and cardiology. The program continues to evolve, with one-year patient survival rates of over 90 percent and more durable graft function with improved patient clinical outcomes due to lower levels of immunosuppression.



The first University of Michigan liver transplant team



Drs. Darrell A. Campbell Jr., Jeremiah G. Turcotte and Donald Dafoe performed the first pancreas and liver transplants at U-M

The first transplant was done August 2,

# 1985

## Keeping the Focus:

### PROVIDING PATIENT-CENTERED CARE TO LIVER TRANSPLANT PATIENTS

Now in its 30th year, the University of Michigan Liver Transplant Program was the first program established in Michigan and one of the first 10 in the United States. Since 1986, the program's faculty have performed more than 2,250 transplants, including more than 350 pediatric liver transplants.

In addition to volume, quality outcomes help differentiate the U-M program. The one-year patient survival rate in the most recent publicly reported cohort reached 91.5 percent, despite a waitlist of increasingly ill patients.

"Our recent outcomes are fairly remarkable in light of the increasing acuity of patients being referred for transplantation," said **ROBERT J. FONTANA, MD**, who served as the Medical Director of the U-M Liver Transplant Program since 2002. The outcomes reflect the work and dedication of a highly coordinated team of medical and surgical experts from multiple specialties and a team

of over 100 staff who touch the life of each individual patient.

#### Improving access to multidisciplinary care

One of the earliest programs to embrace multidisciplinary clinics in the 1990s, the program's hepatologists began seeing patients hand in hand with surgeons, social workers and other practitioners in the outpatient clinic. Working in close collaboration with the surgical director of the liver transplant program, **DR. JOHN MAGEE**, today, the multidisciplinary nature of the program has greatly expanded. Patients can see a hepatologist, surgeon,

social worker, dietitian, pharmacist and nursing coordinator all in one visit.

"Our multidisciplinary clinics were designed to facilitate patient-centered care," said Dr. Fontana. "The individuals who come to us are facing a lot of medical challenges, and we want to make their visits as easy as possible—for them and for their family members alike."

In 2013, toward that same patient-centered goal, the Liver Transplant Program opened a new, state-of-the-art transplant clinic on the first floor of the Taubman Center. The clinic includes nutrition therapy,



phlebotomy, radiology, a pharmacy and facilities for some outpatient procedures, including paracentesis, liver elastography, intravenous infusions and blood transfusions.

#### **Reaching out to Michigan patients and their doctors**

To further facilitate access to care, patients can see the Division's liver specialists through additional Advanced Hepatology clinics, held on the west side of the state in Grand Rapids and Midland in the Thumb area. In addition, Hepatology faculty currently see patients at University of Michigan Health System satellite clinics in Brighton, Northville and Canton to provide more convenient and easier access options for both general hepatology and liver transplant patients.

"Our goal when we establish these clinics is to help the area medical communities provide the best possible care locally," said Dr. Fontana. In addition, a series of Continuing Medical Education (CME) programs focusing on liver disease have been held in various locations throughout the state for the past 20 years to keep practitioners apprised of the latest advances in clinical care and research. "Through the educational programs, local physicians expand their expertise and the services they offer, which they, and their patients, appreciate," he added.

#### **Research findings inform care**

Research being conducted by the Division's faculty guides the care patients receive and provides access to new and experimental treatments. In

the late 1980s, Drs. Michael Lucey and Keith Henley helped define the criteria and process to offer liver transplantation to patients with alcoholic liver disease. These seminal studies have influenced the practice of transplantation over the past 25 years.

Dr. Fontana, an expert in drug-induced liver disease, currently co-chairs two large National Institutes of Health (NIH) research networks, including the Acute Liver Failure Study Group. Patients with acute liver failure (ALF) and drug-induced liver injury have access to the latest therapies to improve their likelihood of survival. The U-M program was a key contributor to a study that demonstrated improved



Robert J. Fontana, MD

transplant-free survival in ALF patients who received IV N-acetylcysteine compared to placebo. Studies utilizing a non-invasive breath test to identify those that will recover with supportive care as soon as possible are currently underway. In addition, studies have been done defining the role of extracorporeal artificial liver support for patients with chronic liver failure in the intensive care unit.

Dr. Fontana and his colleagues have also been involved in a number of pioneering studies on the use of direct-acting antiviral agents (DAAs) to improve the treatment of hepatitis C (HCV), the leading cause of liver failure culminating in transplantation. Fellow Division researcher **DR. ANNA S. LOK**, was the first author of a study reporting the use of DAA

therapy to clear HCV infection, and in 2014 Dr. Fontana treated the first liver transplant recipient with a combination of phase 2 drugs, which have now become the standard of care.

Dr Lok was also the lead investigator for the NIH hepatitis B virus orthotopic liver transplantation (HBV OLT) study that defined the role of oral antiviral agents for patients with HBV both before and after liver transplantation. That work has led to new immunoprophylaxis strategies that are simpler to administer and more convenient for patients. Drs. Lok and Fontana continue to work on better therapies for patients with compensated chronic HBV as well in the context of the ongoing NIH Hepatitis B Research Network.

The U-M Liver Transplant Program is also a leader in the conditioning of donor organs, including extracorporeal membrane oxygenation perfusion for organs from high-risk donors. A clinical trial with 10 other transplant sites is also being started on normothermic extracorporeal perfusion.

"If successful, this novel approach could enable us to substantially expand the donor supply and provide transplants to more patients, saving a lot more lives," said Dr. Fontana.

Other studies are underway to develop parameters for pre-operative risk assessments and to reduce the amount of blood products needed for transfusion using rotational thromboelastometry (ROTEM).

Faculty in the U-M Liver Transplant Program are active in policy development related to transplantation, and U-M recently served as headquarters for the Scientific Registry of Transplant Recipients. Research protocols offering the latest treatments for patients with hepatitis B, alcoholic hepatitis and cholangiocarcinoma are underway.

The U- M program has also been a leader in the use of radiation therapy and other neo-adjuvant treatments for the management of patients with liver cancer that have led to improved outcomes and more patients becoming eligible for transplant.

"We work on many fronts to advance the field," said Dr. Fontana, "and that enables us to keep fully focused on always improving the care we provide to all our patients."

**George Magulak, DDS**

FEELING "BLESSED WITH GOOD FORTUNE AND EXTRAORDINARY CARE"

**After George Magulak, DDS, was diagnosed with primary biliary cholangitis (PBC) in 2004 during a routine physical and blood test, he threw himself into learning as much as he could about this rare autoimmune disease.**

Determined to stave off the damage that necessitates liver transplant, Dr. Magulak changed his diet and exercise routines to better support his liver, and continued seeing patients in his busy Michigan dental practice. He hiked, golfed and skied with family and friends.

In 2011, signs of advancing disease began emerging, although doctors didn't think they were related to PBC.

Soon after, Dr. Magulak met Dr. Robert Fontana, Medical Director of the University of Michigan Liver Transplant Program at an organ donation fundraiser. Following the event, Dr. Fontana reviewed Dr. Magulak's records and delivered dire news: he was going to need a liver transplant and needed to get onto the waiting list right away.

Dr. Magulak was accepted to the transplant list at U-M and later at the Medical University of South Carolina. He wrote a letter to his patients, sold his practice and moved south, believing the likelihood of being selected was

better there, given the lower demand for organs in the region.

Rapidly deteriorating, Dr. Magulak received a call one morning at his hotel room in South Carolina from a former patient. The son of a family friend of another patient, who had died in a car crash in Michigan, was made aware that the young man's family wanted to direct the donation of his organs. The patient remembered his dentist's moving letter and tracked down Dr. Magulak.

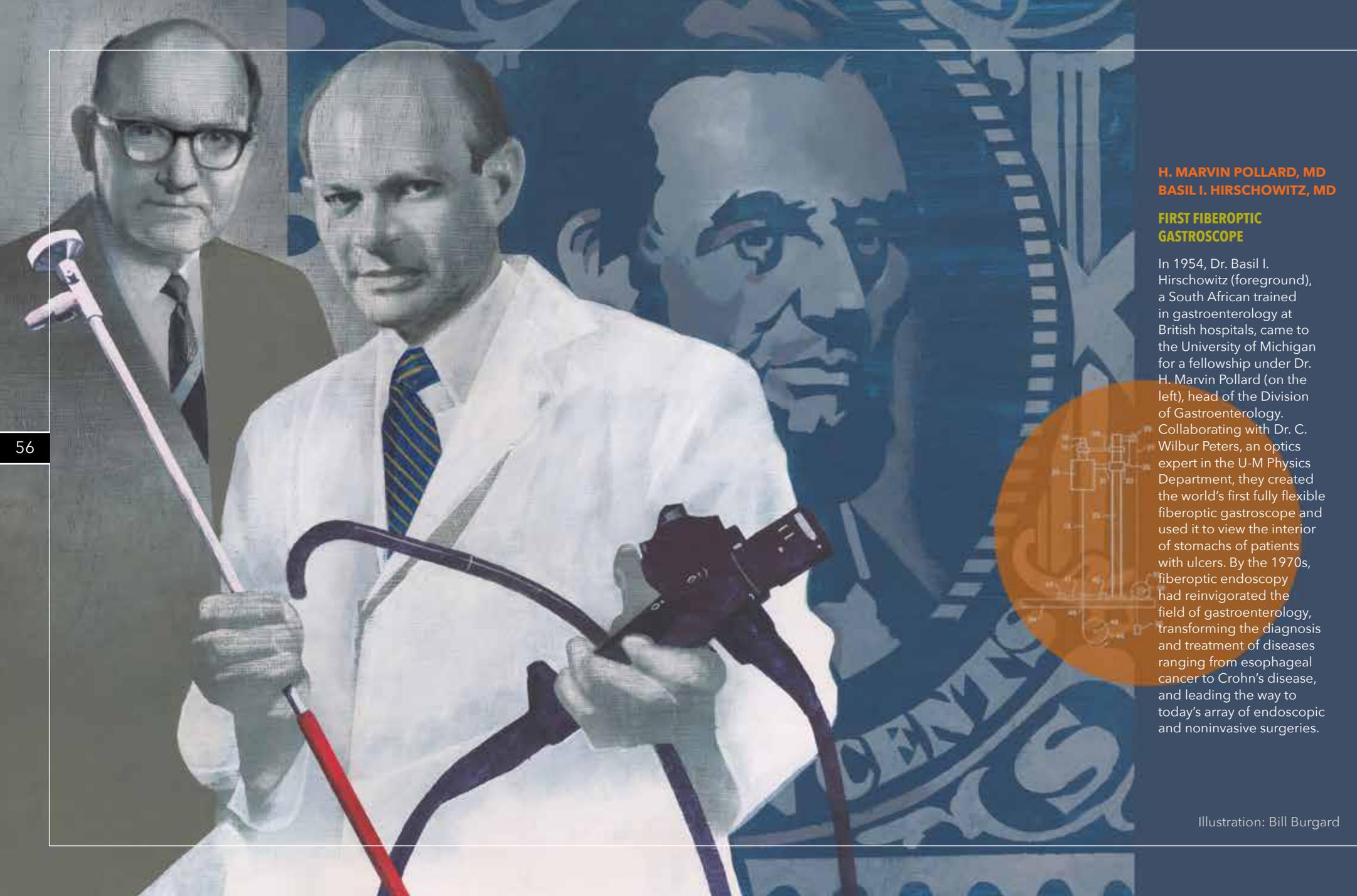
After the U-M transplant coordinator called hours later, Dr. Magulak boarded a plane and arrived in Ann

Arbor at 3 a.m. He received a new liver that day.

Nearing the one-year anniversary of the transplant, Dr. Magulak is optimistic and grateful to the donor and family who saved his life and to the U-M Liver Transplant Program. "The hepatology and transplant team has treated me with the utmost empathy, respect and professionalism...They included me in every decision concerning my care. I feel very blessed with the good fortune and extraordinary care I've had."



**Patient Story**



**H. MARVIN POLLARD, MD**  
**BASIL I. HIRSCHOWITZ, MD**

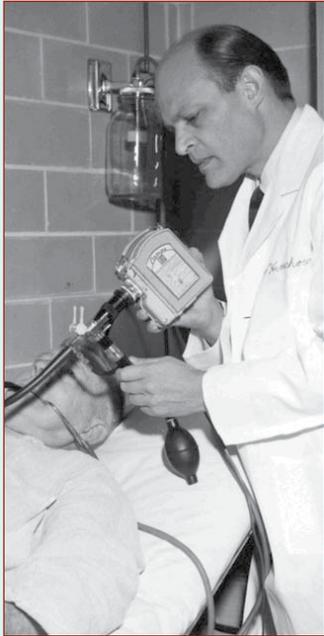
### **FIRST FIBEROPTIC GASTROSCOPE**

In 1954, Dr. Basil I. Hirschowitz (foreground), a South African trained in gastroenterology at British hospitals, came to the University of Michigan for a fellowship under Dr. H. Marvin Pollard (on the left), head of the Division of Gastroenterology. Collaborating with Dr. C. Wilbur Peters, an optics expert in the U-M Physics Department, they created the world's first fully flexible fiberoptic gastroscope and used it to view the interior of stomachs of patients with ulcers. By the 1970s, fiberoptic endoscopy had reinvigorated the field of gastroenterology, transforming the diagnosis and treatment of diseases ranging from esophageal cancer to Crohn's disease, and leading the way to today's array of endoscopic and noninvasive surgeries.

Illustration: Bill Burgard

## Medical Procedures Unit:

BUILT UPON A FOUNDATION OF INNOVATION



Basil Hirschowitz, MD, PhD

Established in 1991 under the leadership of **DR. TACHI YAMADA**, then division chief, and **DR. TIMOTHY NOSTRANT**, acting chief prior to Dr. Yamada, the University of Michigan Medical Procedures Unit (MPU) serves patients from all over Michigan and the Midwest.

The MPU is built upon a solid history of innovation in endoscopy within the Division of Gastroenterology. In 1957, **DR. BASIL HIRSCHOWITZ** led the team that invented the first flexible fiberoptic endoscope. In 1961 **DRS. ROBERT BOLT** and **ARTHUR FRENCH** demonstrated a simplified multiple-retrieving small bowel biopsy tube that enabled them to perform the first small bowel biopsy and seminal research on the association between small bowel morphology and malabsorption.

Today, the MPU provides a number of routine and, increasingly, more advanced diagnostic and therapeutic procedures, including balloon-assisted endoscopy, capsule endoscopy,

esophageal endoscopic mucosal resection, endoscopic retrograde cholangiopancreatography, endoscopic ultrasound and liver biopsy, among many others.

Comprising 11 endoscopy rooms, two procedure rooms for fluoroscopy and the GI Physiology and Manometry Laboratory—as well as several satellite procedure units at other U-M Health System centers—MPU facilities performed some 30,000 procedures in 2016.

“The MPU was one of the first ‘modern’ endoscopy units in the country. It was a real showcase,” said **GRACE ELTA, MD**, MPU director since 2002. “And it

has been critical to our GI Division since more than 50 percent of our clinical activity is endoscopy, and much of the endoscopy training for our fellows occurs in the MPU.”

A full-time endoscopy research coordinator facilitates many studies in the MPU, and the Unit will support clinical studies of new endoscope systems and peptide probes developed by Professor **THOMAS WANG, MD, PhD**. In work published in the *New England Journal of Medicine* (2012; 366: 1414-1422), MPU investigators found that a single prophylactic dose of indomethacin administered immediately post-procedure can significantly reduce the risk of

developing ERCP-induced pancreatitis, which occurs in about 15 percent of high-risk patients undergoing the procedure, and 5-10 percent of average-risk patients. This has become the standard of practice in most medical centers.

“Ongoing research and clinical advances nurtured by the MPU have supported greater numbers of complex procedures being performed on patients who require more complicated care, and we expect this trend to continue since the University of Michigan is a major referral center for gastrointestinal diseases,” said Dr. Elta.



Grace Elta, MD

## Motility Disorders:

BRINGING SCIENTIFIC DISCOVERY TO PATIENT CARE

With 10 faculty specializing in research and treatment of motility disorders, the U-M Motility Disorders Group (MDG) is the largest and one of the most versatile groups of motility experts in the country. The group includes **JOHN W. WILEY, MD** (visceral hypersensitivity and IBS), **WILLIAM D. CHEY, MD** (food allergy and IBS), **WILLIAM HASLER, MD** and **ALLEN LEE, MD** (gastroparesis), **BORKO NOJKOV, MD** (non-ulcer dyspepsia), **RICHARD SAAD, MD, MSc** (pelvic floor disorders and colonic inertia), **STACY MENEES, MD, MSc** (women's health and pelvic floor disorders), **SHANTI ESWARAN, MD** (low-FODMAP diet and IBS), **JOEL RUBENSTEIN, MD, MSc** (esophageal motility disorders, GERD and Barrett's Esophagus) and **CHUNG OWYANG, MD** (intestinal pseudo-obstruction, microbiome and IBS).

Most of our motility experts are opinion leaders in their subspecialties and provide care through several specialized clinical programs. The gastroparesis program is a key participant in the National Gastroparesis Registry and specializes in innovative treatments of refractory gastroparesis and cyclic vomiting. Up to 30 percent of patients seen in the GI outpatient service have irritable bowel syndrome (IBS). Many are difficult

cases referred from other gastroenterologists. Using a holistic approach, our IBS experts achieve a high rate of success in treatment.

The U-M GI Motility Disorders Program was the first to use Octreotide to treat intestinal pseudo-obstruction. Currently large populations of intestinal pseudo-obstruction patients come from all regions of the United States to seek innovative treatments for this group of difficult motility

disorders. In collaboration with our surgical colleagues and using state-of-the-art technology offered by the GI Physiology and Manometry Laboratory, the U-M Motility Program treats numerous patients with slow transit constipation who do not respond to traditional laxatives. The Michigan Bowel Control Program uses a multidisciplinary approach to treat pelvic floor disorders and sphincter abnormalities.

### GI Physiology and Manometry Laboratory

The GI Physiology and Manometry Laboratory under the leadership of Dr. William Chey and Jason Baker is located in the Medical Procedures Unit (MPU). The lab performs unique diagnostic tests for patients with motility disorders:

- Comprehensive diagnostic technology including video capsule, smart pill and colon capsules.
- Electrogastrography (EGG) monitors gastric pacemaker activities and is used as a tool for the diagnosis of tachygastric arrhythmias, a condition often observed in patients with nausea and vomiting.

- GI manometric studies record gastrointestinal motility and help diagnose intestinal pseudo-obstruction and to differentiate neuropathic from myogenic disorders.

These tests are not available in many medical centers in the United States, and only the University of Michigan offers all three in one location.

#### Coordinated Team approach

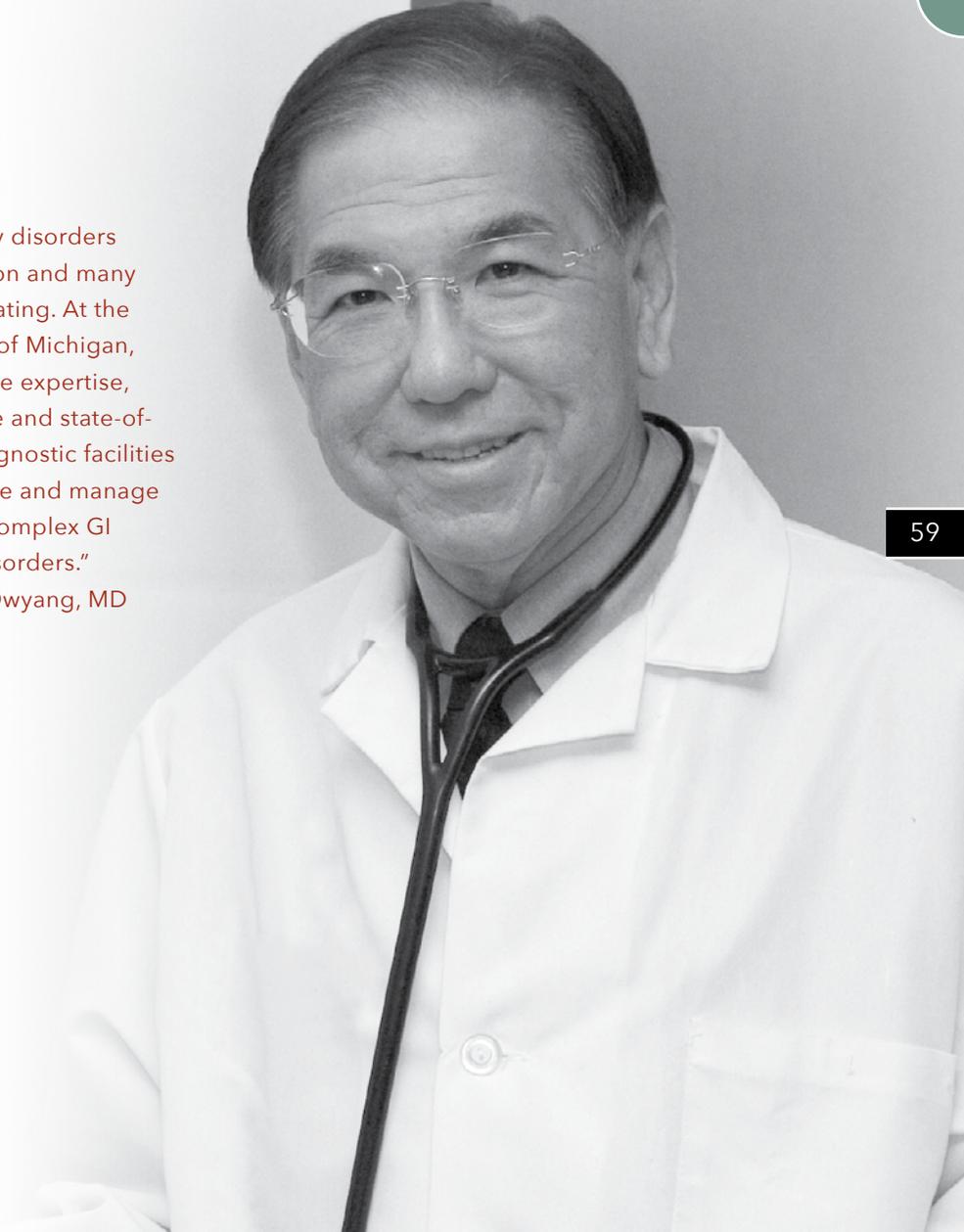
A team of experts from different disciplines provides optimal care for patients with difficult motility disorders. The Department of Gastrointestinal Surgery provides services such as placement of pacemakers in the stomach and insertion of intestinal feeding tubes for refractory gastroparesis. Two registered dietitians

(RDs) with specialized knowledge in low-FODMAP diets evaluate nutritional needs and recommend dietary changes to reduce symptoms. The RDs also recommend enteral and parenteral nutrition regimens when needed. The program's behavioral psychologist specializes in the management of chronic pain and can provide behavior therapy and hypnosis. Our physical therapists have specialized knowledge in pelvic floor disorders and anal sphincter abnormalities and work with patients suffering from pelvic muscle dyssynergia and fecal incontinence.

#### Research and Innovation

With strong National Institutes of Health research funding, physicians and physician scientists within the

“GI motility disorders are common and many are debilitating. At the University of Michigan, we have the expertise, experience and state-of-the-art diagnostic facilities to diagnose and manage the most complex GI motility disorders.”  
– Chung Owyang, MD



MDG have contributed to the scientific literature in many ways, including demonstration of new therapies and treatment approaches, all of which improve the lives of patients cared for in the Motility Disorders Clinic.

"Our inquiries into the underlying causes of these disorders and how best



William Hasler, MD

to treat them mean that we have been quite successful in addressing some very complex issues for our patients," said Dr. Owyang, who heads the group and the Motility Disorders Clinic.

#### **New approaches to motility failure**

Since many motility disorders have neurological underpinnings, they can be extremely difficult to diagnose and treat. The group uses its unique expertise: original clinical research, frequent clinical and drug trials and state-of-the-art diagnostic equipment and procedures to provide new treatments and therapies to these patients.

Work related to intestinal pseudo-obstruction, conducted by Dr. Owyang in the early 1990s, led to the use of Octreotide to treat the

disorder—the first time a gut peptide had been used to treat a GI disorder (*New England Journal of Medicine*, 1991; 325:1461-1467). More recently, Dr. Chey's research indicates that Naloxegol may be beneficial to treat opioid-induced constipation (*New England Journal of Medicine*, 2014; 370: 2387-2396). Similarly, Dr. Hasler's clinical interest in diabetic gastroparesis has led to the exploration of new possibilities for electronic pacing of the stomach.

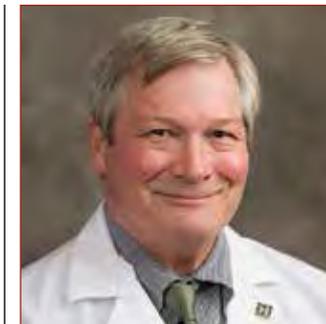
#### **Solving the puzzle of functional bowel disease**

New research at the University of Michigan is also leading to the use of diet as form of treatment for irritable bowel syndrome (IBS) in many patients. Drs. Chey and Eswaran have published the first rigorous clinical

trial showing that a low-FODMAP (fermentable, oligosaccharides, disaccharides, monosaccharides and polyols) diet can improve symptoms and quality of life for patients with IBS (*Gastroenterology*, 2016; 150 (4): S172).

"We're achieving cure rates on the order of 70 to 75 percent using diet alone," said Dr. Owyang.

Work by the Motility Disorders Group investigators is also continuing to point to abnormalities in gut bacteria, or dysbiosis, as a cause of IBS. Researchers are looking at host-microbiome interactions to better understand how the microbiome affects motility, regulates permeability of the GI tract's mucosal lining and affects mood, including the depression and anxiety commonly experienced by IBS



John W. Wiley, MD

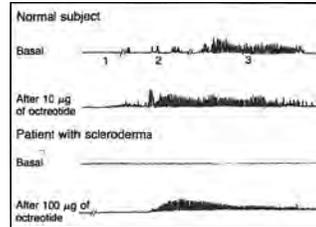
patients. The findings are informing the use of antibiotics and probiotics to treat the disorder.

"The microbiome as a target of therapy is the subject of several investigations," said Dr. Owyang. "It's a telling example of how research is driving our clinical practice."

“Work performed by the motility group led to the discovery of new drugs for the treatment of GI motility disorders. These discoveries significantly impacted clinical practice, becoming the standard of practice for treatment of this group of GI disorders” – Chung Owyang, MD

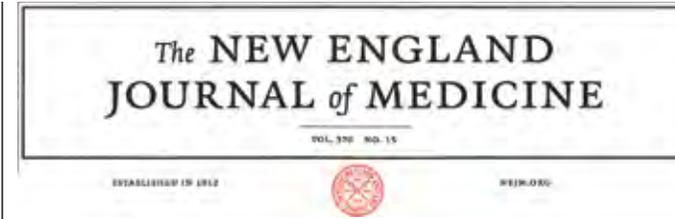


Back row: Mark McDermott, Jacob Kurlander MD, Jason Baker  
Front row: Kathy Dayne, Joel Rubenstein MD, MSc, William D. Chey MD, Joan Chen MD, MSc, Hanan Al-Shahly



Intestinal Manometric Tracings in a Normal Subject and a Patient with Scleroderma.

The manometric recordings in normal subjects showed propagative intestinal patterns during fasting. In contrast, the patients with scleroderma who had pseudoobstruction and bacterial overgrowth did not have any spontaneous duodenal phase 3 activity. Octreotide evoked intestinal phase 3 complexes that were qualitatively similar to the complexes evoked by octreotide in the normal subject. This observation eventually led to the use of octreotide to treat patients with intestinal pseudoobstruction.

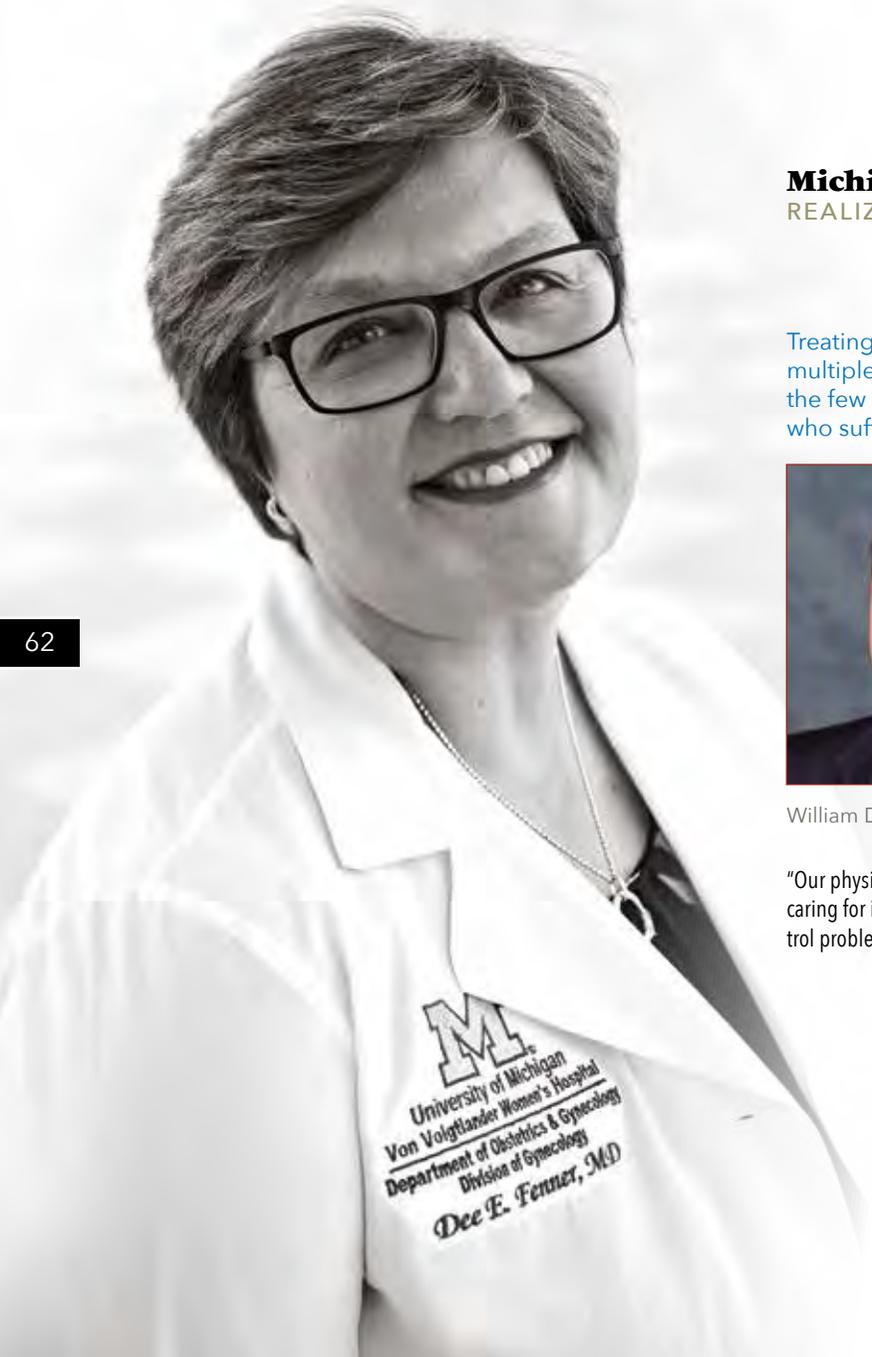


#### Effect of Octreotide on Intestinal Motility and Bacterial Overgrowth in Scleroderma

Hani C. Soudah, MD, William L. Hasler, MD, and Chung Owyang, MD  
*N Engl J Med* 1991; 325:1461-1467 November 21, 1991 DOI: 10.1056/NEJM199111213252102

#### Naloxegol for Opioid-Induced Constipation in Patients with Noncancer Pain

William D. Chey, MD, Lynn Webster, MD, Mark Sostek, MD, Jaakko Lappalainen, MD, PhD, Peter N. Barker, PhD, and Jan Tack, MD, PhD  
*N Engl J Med* 2014; 370:2387-2396 June 19, 2014 DOI: 10.1056/NEJMoa1310246



## Michigan Bowel Control Program

REALIZING A VISION FOR COORDINATED CARE AND RESEARCH ACROSS DISCIPLINES

Treating bowel control problems such as severe constipation and fecal incontinence involves multiple specialties and treatment approaches. The University of Michigan is home to one of the few programs nationwide to offer highly coordinated, multidisciplinary care to patients who suffer from bowel control disorders.



William D. Chey, MD

“Our physicians not only are experts in caring for individuals with bowel control problems; they’re also conducting

research into causes and treatments and developing novel approaches to helping our patients,” said **WILLIAM D. CHEY, MD**, who co-founded the Michigan Bowel Control Program (MBCP) program in 2005 and currently serves as medical director.

Dr. Chey and colleagues **DEE FENNER, MD**, a professor of gynecology, and **RICK SAAD, MD**, Associate Professor of Medicine, specializing in constipation and pelvic floor disorders, established the program to carry out their vision: to break down siloes and bring together a team of specialists—



Rick Saad, MD, MS

gastroenterologists, urogynecologists and colorectal surgeons—who would provide innovative approaches to

diagnosing, managing and treating bowel control disorders in their patients. Other gastroenterologists working in the MBCP include **DRS. SHANTI ESWARAN, ALLEN LEE, STACY MENEES** and **BORKO NOJKOV**.

“We knew we could do better for our patients if we put our heads together and developed coordinated, fully integrated care plans,” said Dr. Chey.

The program has grown tremendously over the past 16 years, from about 50 new patient referrals the first year to more than 500 in 2015. Patients have come from all across the United States and other countries as well.

Follow-up care is a critical part of the MBCP’s work. A dedicated team



Stacy Menees, MD, MSc of nurse concierges helps patients implement and follow their care plans, all essential steps toward improving outcomes. Rigorous scientific and clinical research by MBCP faculty also contributes to advancements in care. Dr. Chey, in collaboration with

gastroenterologist **STACY MENEES, MD**, is leading a trial comparing dietary fiber supplementation to a low-FODMAP diet (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) for the treatment of fecal incontinence. Trials also are underway for a novel glove-based manometry system Dr. Chey developed for the evaluation of anal sphincter function.

"When we established the MBCP," Dr. Chey said, "we set out to continually improve the care we deliver by bringing disciplines together and digging deeper into why patients suffer from the symptoms they do. As a result, we continually gain new insights into better and better ways to help resolve them."

Using a model of the pelvis, Dr. Fenner, with nurse Anne Mcleod, helps a patient understand the relationship between constipation and pelvic organ prolapse.





William D. Chey, MD

## Solving the Puzzle of IBS: A NEW STANDARD OF CARE EMERGES

Successful management of irritable bowel syndrome (IBS) requires a comprehensive approach to care that combines the expertise of multiple health care professionals who specialize in dietary and behavioral counseling, in addition to medical treatments and pharmaceutical therapies.

"Over the last five years, we have identified and assembled the puzzle pieces that allow us to offer a more holistic approach to patients with IBS," said **WILLIAM D. CHEY, MD**, who is a widely known expert on IBS.

That means thinking critically about how diet, lifestyle and behavior might interact to bring about the symptoms of IBS. "We consider how we might offer interventions for each of those components of care to really maximize the benefit of medical treatments for patients with IBS," he said.

"If you asked any of the gastroenterologists at the University of Michigan five years ago, diet and behavior would have been very low on their list of priorities," Dr. Chey said. "Now, our gastroenterologists say they can't imagine how we did it before we had these assets in place. It has really been a transformation in care over the past five years, and we're extremely proud of that."

Successful long-term management of IBS, it turns out, is a multidisciplinary affair.

### Puzzle Piece A: Expert Dietary Counseling

For many patients, symptoms of IBS are triggered by what they eat, and increasingly, physicians are recognizing the critical role of diet in managing the symptoms of IBS. Unfortunately, few physicians are trained to provide nutritional counseling.

"The reality is most gastroenterologists receive little to no training in nutrition or the practical elements of administering diet therapies for patients with IBS," Dr. Chey said.

Emerging evidence suggests diets free of gluten and diets low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols—commonly known as the low-FODMAP diet—can be beneficial for patients with IBS. The low-FODMAP diet, in particular, is a fairly complicated diet, Dr. Chey noted. Patients following this diet require the assistance of professional nutrition specialists.

"I think most physicians right now are trying to manage diet by giving patients a sheet of paper with a list of foods to eliminate, and that's simply inadequate," he said. "Diets are definitely more comprehensive and complicated than can be conveyed with a sheet of paper—even potentially dangerous if not administered in a medically responsible way."

As a result, many diets do not work as well in clinical practice as evidence from clinical trials might suggest, he noted. In order to achieve similar results, diets need to be administered by experts who understand gastrointestinal nutrition and know how to help patients incorporate dietary changes into their daily routines, he said.

"One of the problems right now is there aren't that many trained GI dietitians around. There are dietitians, but they're not specially trained in gastroenterology," Dr. Chey said.

"One of the things that needs to happen on a national level to improve the quality of care for patients with IBS is to train a population of dietitians that have expertise in GI disorders, and to have them work closely with

gastroenterologists to administer dietary interventions in a medically responsible way," he added.

This is just one of the many areas where the University of Michigan sets itself apart: the Division of Gastroenterology has the equivalent of four GI dietitians—two full-time GI dietitians at University Hospital and others who assist in caring for patients at offsite facilities that are part of the University of Michigan Health System.

### **Behavioral Therapies Found Instrumental for IBS Management**

The Behavioral Health Program at the University of Michigan offers patients with GI disorders an opportunity to address symptoms with a specially trained GI psychologist.

**MEGAN RIEHL, PsyD**, is a clinical health psychologist at the U-M, and the state's only psychologist with a specific focus on GI disorders. IBS is the most common GI illness that brings patients to her clinic. "About 65 percent of patients present with IBS or a functional bowel disorder," she said.

Typically, patients are referred to Dr. Riehl by a gastroenterologist who may have exhausted medical treatment options and/or believes a patient would benefit from stress and anxiety management techniques. Increasingly, behavioral therapy is becoming routine in the treatment of patients with IBS. "As more patients become aware of the GI behavioral health service, more of them are asking their gastroenterologists for a referral to the program," Dr. Riehl said.



Dr. Megan Riehl explains to a patient about brain-gut interaction.

Behavioral therapy is personalized for each patient, but in general, therapy is designed to help patients deal with the “uncontrollable” and “unpredictable” aspects of IBS. Patients learn relaxation and stress management techniques they can apply to everyday life stressors.

“My goal is to help patients learn to cope effectively and efficiently with worries that can interfere with social, occupational and family life,” Dr. Riehl said.

#### **Gut-Directed Therapies**

Most often, behavioral therapy for patients with IBS involves interventions based on cognitive-behavioral therapy (CBT), a short-term, collaborative treatment that is focused on a patient’s current problems.

“CBT involves helping patients find new ways of thinking and behaving to help manage stressful situations,” Dr. Riehl explained. For example, patients with IBS may experience anxiety-provoking thoughts such as, “Where will a bathroom be if I need it?,” “What if I’m having symptoms before a big exam or presentation?” or “How will I ever be intimate with a partner?” CBT teaches patients how to manage emotional responses to these potentially stress-inducing situations.

“My goal is to aid patients in self-management strategies that benefit GI health, emotional well-being and overall quality of life,” Dr. Riehl said. “People learn tools to create long-term change, without remaining in treatment for long periods of time. It’s very rewarding.”

#### **Puzzle Piece B: Focused Behavioral Therapy**

Just as diet has come into focus as an essential aspect of treatment for IBS, so have behavior and lifestyle. The way in which an individual responds to stress can greatly affect symptoms of IBS.

“There are certainly some things that gastroenterologists can recommend to try to facilitate changes in lifestyle or behavior,” Dr. Chey said. For example, yoga or a regular exercise plan can be very helpful in managing stressors that can lead to the symptoms of IBS.

But as in the case of diet, many gastroenterologists are not trained to provide more advanced behavioral counseling to patients with IBS.

For example, cognitive-behavioral therapy, hypnosis and interpersonal psychotherapy can be very beneficial for patients with IBS. But these therapies require specialized training—even more specialized than many clinical psychologists are equipped to offer.

#### **Puzzle Piece C: Medications and Research**

“Medications still play the really important role,” Dr. Chey noted.

Therapy for IBS is symptom-driven, depending on a patient’s needs. “For patients with mild or moderate IBS symptoms, sometimes all they need is a little bit of medication, such as an over-the-counter antidiarrheal or antispasmodic on an as-needed basis, and they’ll do just fine. Patients with more severe IBS symptoms will almost

## LOW-FODMAP DIET

always need one or more medications," Dr. Chey said.

Notably, Dr. Chey's group has been involved in some capacity in the research that led to the FDA approval of all five prescription drugs indicated for the treatment of IBS in the United States.

Because of its dedication to research, the University of Michigan gives its patients the opportunity to participate in ongoing IBS clinical trials, such as those involving the low-FODMAP diet and an upcoming trial of prebiotics in patients with IBS.

Building on this foundation in GI nutrition and behavioral therapy, a new effort—the Digestive Disorders Nutrition and Lifestyle Program—will bring together the diverse elements

necessary to provide support in nutrition and behavior, as well as "vertically integrate research from the bench to the bedside," Dr. Chey said. "So we're not only providing excellent quality of care for patients, we're also striving to make discoveries that will transform the role of diet and behavior and how they interact with medications to maximize benefit for patients with IBS and other functional disorders."

*"I think most physicians right now are trying to manage diet by giving patients a sheet of paper with a list of foods to eliminate, and that's simply inadequate."*

— William D. Chey, MD

### MEATS

#### AVOID

- Chorizo
- Sausages
- Processed meat

#### ENJOY

- Beef
- Chicken
- Lamb
- Pork
- Turkey
- Seafood

### DAIRY AND EGGS

#### AVOID

- Milk
- Sour cream
- Yogurt
- Cream cheese
- Ice cream

#### ENJOY

- Lactose-free milk
- Lactose-free yogurt
- Butter
- Cheese
- Eggs

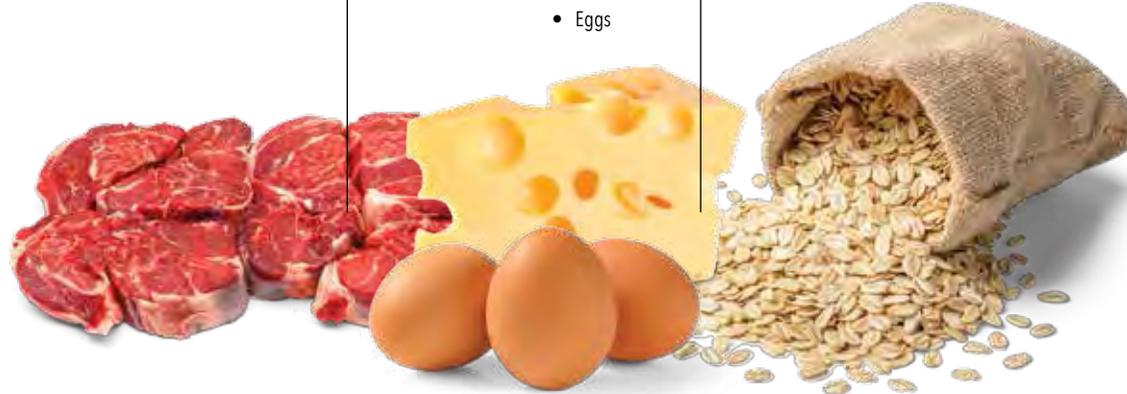
### GRAINS

#### AVOID

- Wheat (gluten)
- Barley
- Bran cereals
- Rye
- Semolina

#### ENJOY

- Gluten-free baked goods
- Brown rice
- Oatmeal
- Quinoa
- Corn tortilla



## LOW-FODMAP DIET

### FRUITS

#### AVOID

- Apples
- Avocado
- Cherries
- Grapefruit
- Peaches

#### ENJOY

- Bananas
- Blueberries
- Cantaloupe
- Grapes
- Lemon



### CONDIMENTS

#### AVOID

- Honey
- Jam
- Pesto sauce
- Relish
- Stock cubes

#### ENJOY

- Mustard
- Ketchup
- Barbecue sauce
- Chocolate
- Mayonnaise
- Peanut butter



### LEGUMES

#### AVOID

- Kidney beans
- Lima beans
- Butter beans
- Black beans
- Split peas
- Soy beans

#### ENJOY

- Chick peas
- Lentils



### VEGETABLES

#### AVOID

- Garlic
- Onions
- Cauliflower
- Celery
- Mushrooms

#### ENJOY

- Carrots
- Green beans
- Lettuce
- Bell peppers
- Squash

Patients following this diet require the assistance of professional nutrition specialists.

## Morgan's Story

Morgan Blenkhorn missed high school several times because of symptoms that doctors said were related to irritable bowel syndrome (IBS).

"Anything I would eat, I would get sick," she said. "I was nauseous; I would have headaches, stomach-aches; I had diarrhea and I was just ill all day, every day."

Morgan's symptoms started a few months after a severe food poisoning incident in 2010 during her junior year of high school. She endured pain, particularly while dancing and playing soccer. She eventually turned to apples and honey for relief, but they only made her symptoms worse.

"It was really hard having to come home from school being sick all the time, waking up sick and trying to go to school and act like everything was fine," she said.

### A Chance Meeting Bears Fruit

Over the next three years, several doc-

tors told her she was exhibiting IBS symptoms and gave her probiotics for treatment. But a chance meeting on an airplane between her father and gastroenterologist William Chey, MD, would lead to a series of interviews, tests and a final diagnosis from the University of Michigan's gastroenterology and dietitian team.

Her first visit to the University of Michigan was in 2013, during the fall of her sophomore year of college. She had several blood tests done before meeting with Dr. Chey. Upon her first appointment with him, she was promptly told what to expect: a fructose test, a lactose test, more blood tests and an endoscopy.

According to Morgan, Dr. Chey went above and beyond preliminary tests to find the root of the problem. The test that changed it all, she said, was the fructose test, which consisted of a fruc-

tose mixture, water and a breath test. A few weeks after her appointment, Dr. Chey spoke with Morgan and her family and told them the diagnosis: fructose intolerance.

"We all cried," Morgan said.

### Finally, Control ...

This experience was unlike any other for Morgan. The team's gastroenterologists were briefed on her case and knew exactly how to address her issues. The dietitian they referred her to mapped out a zero-fructose eating plan that catered to her vegetarian diet and her love for veggies, pasta and curry.

"They listened to my specific wants, not just me as a patient but me as Morgan," she said.

After being diagnosed with fructose intolerance, Morgan now plans her own meals and has full control of her

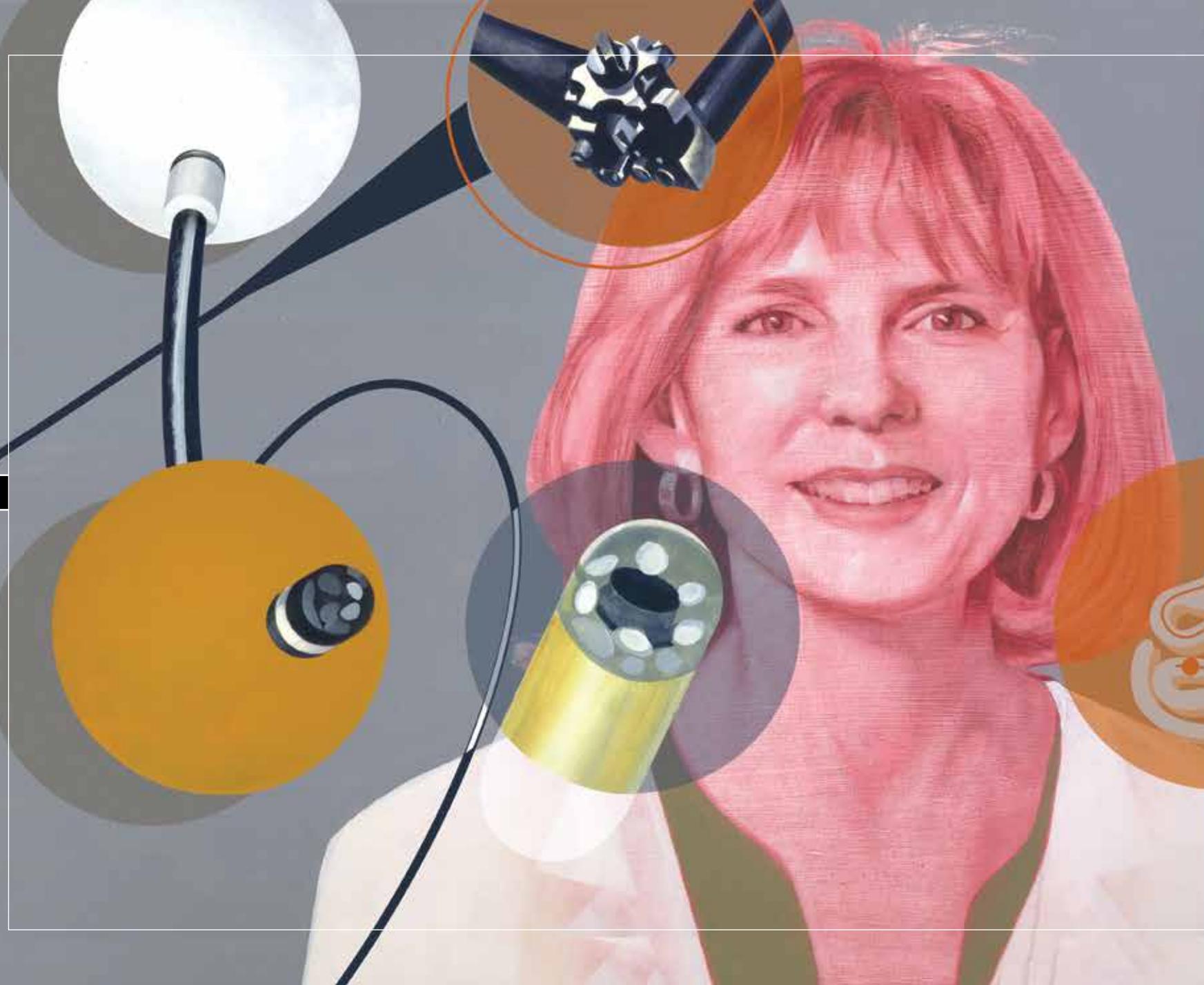
symptoms. She continues to dance and play sports. Last summer, she was even able to study abroad in the Netherlands.

"It was beautiful, life-changing, something I didn't think I'd ever be able to do before because I couldn't sit in a car for two hours without having to pull over," she said. "Biking 10 miles to work and backpacking alone through Germany were things I thought I'd never be able to do because I was so sick."

Morgan is finishing her fourth year at Grand Valley State University in Allendale, Michigan, with another year left to complete her special education degree. She still checks in with Dr. Chey every once in a while. For now, she hopes to be accepted into Grand Valley's Consortium for Overseas Student Teaching program in Ireland this summer.



# Patient Story



**LAUREL R. FISHER, MD**

**SMALL BOWEL PROGRAM:  
CAPSULE ENDOSCOPY  
AND BALLOON-ASSISTED  
ENTEROSCOPY**

An early pioneer in small bowel imaging technology, the Division of Gastroenterology at the University of Michigan first offered capsule endoscopy to patients in 2001, rapidly becoming a national leader in the field of small bowel enteroscopy. In 2007, the Division performed the first therapeutic double-balloon enteroscopy in the state of Michigan, and the University of Michigan remains the only referral center statewide. To date, the Division has performed over 5,300 capsule endoscopy and nearly 2,000 double balloon procedures and is poised to continue its commitment to advanced technology for enhancing patient care.

Illustration: Bill Burgard

## Small Bowel Disorders Program

CUTTING-EDGE PROCEDURES TRANSFORM PATIENT CARE

"The only comprehensive small bowel program in the state, the University of Michigan Small Bowel Disorders Program (SBDP) is transforming how patients with small bowel problems are diagnosed and treated—and changing their quality of life in the process."—Dr. Laurel Fisher, First Director of the Michigan Small Bowel Program

### Capsule endoscopy to visualize the small bowel

Since 2001, the SBDP has been performing video capsule endoscopy (VCE) studies in order to view the approximately 20- to 25-foot-long small intestine for diagnostic purposes. The program's physicians have performed over 5,300 studies, one of the highest volumes in both the state and the nation, according to **MICHAEL RICE, MD**, director of the Small Bowel Disorders Program.

In addition to performing VCE for outpatients, physicians are increasingly performing VCE studies on inpatients,

particularly those with suspected GI bleeding. This often changes the in-hospital care patients receive—and helps to prevent future hospitalizations.

### Double-balloon enteroscopy for diagnosis and treatment

Once the source of bleeding is found through VCE, many patients undergo double balloon enteroscopy (DBE). This intervention is used for both diagnostic and therapeutic purposes, including biopsy, removal of lesions and dilation of strictures. DBE has changed the paradigm of small bowel disease management; many of the SBDP's patients are now able to be en-

doscopically treated, thereby avoiding conventional surgery.

The U-M SBDP is the only tertiary referral center in the state offering DBE. To date, physicians have performed



Dr. Mimi Takami





nearly 2,000 procedures over the past 10 years, among the highest volume in the country. The program employs four DBE enteroscopists and continues to expand., **DRS. MIMI TAKAMI, MICHAEL RICE, NEIL SHETH** and **ANDREW READ**.

"DBE is an important tool in the armamentarium to manage patients with suspected GI bleeding, since small bowel bleeding accounts for about 5 to 10 percent of those cases," said Dr. Rice. "Using VCE to evaluate our inpatients soon after presentation affords the opportunity to identify the source of bleeding early on. As a result, we can capitalize on the opportunity to have a patient undergo an endoscopic therapeutic procedure with DBE during the same hospital stay."

For a decade, specialized endoscopists at U-M have used DBE to successfully evaluate the small intestine to manage small bowel bleeding, tumors, inflammatory bowel diseases and other small intestinal conditions. Increasing numbers of patients with complicated post-surgical altered anatomy, including Roux-en-Y gastric bypass anatomy, are referred to U-M for DBE to assist in the evaluation and management of disorders involving bypassed segments of bowel.

"DBE has revolutionized our ability to provide therapeutics in the management of this growing patient population," said Rice.

Specialized endoscopists in the U-M SBDP have been able to visualize and provide therapy for complications

including bleeding in the bypassed portions of the stomach, duodenum and beyond the jejunum-jejunostomy, which are typically well out of reach of traditional endoscopes. The DBE platform also enables successful negotiation of the sharp angulations of the bypassed intestine to facilitate DBE-assisted ERCP to address bile duct stones and other pancreaticobiliary disorders.

Physicians in the U-M SBDP have helped Crohn's disease patients with small bowel strictures avoid surgery and the subsequent risks of short bowel syndrome. Using DBE, endoscopists have successfully performed stricture dilation using a controlled radial expansion balloon through the lengthy enteroscope. The procedure has helped numerous patients

tolerate advancement of their diet, improve their quality of life and limit their need for surgery.

In addition, patients with Peutz-Jegher's Syndrome (PJS) develop multiple large hamartomatous polyps throughout their small intestine and are at risk for many complications. Using DBE, U-M specialists can proactively and successfully resect these large polyps endoscopically via an oral, rectal or bi-directional approach. DBE with polypectomy has helped patients avert the complications of PJS including intussusception, GI bleeding as well as the risks of surgery and short-bowel syndrome.

DBE is a complex procedure that takes a significant amount of time to perform and requires a high degree

of expertise. Faculty from institutions throughout the country have come to the U-M SBDP to gain that expertise from the program's highly specialized physicians. Training on both VCE and DBE are also being incorporated into GI fellowship training.

#### **At the forefront of endoscopic research**

The SBDP's large database of VCE and patient data is providing an important platform upon which to conduct research, and studies have described and defined indications for VCE use in patients with celiac disease, small bowel strictures and suspected small bowel bleeding. In the near future, the SBDP also will be participating in a multi-center clinical trial involving colon capsule endoscopy.

"It takes a dedicated and comprehensive program to best help patients and to advance the field," said Dr. Rice. "In the not-so-distant past, prior to VCE and DBE, patients with small bowel disorders lived with recurrent hospitalizations, blood transfusions and the resignation that this suffering was inherent in their condition. Now, because of programs like this one, we're able to offer our patients endoscopic options that can make a big difference in their quality of life."



Michael Rice, MD



Peter Higgins, MD, PhD, MSc

## Inflammatory Bowel Disease Program

GROWTH ENHANCES PATIENT-CENTERED CARE AND ACCESS TO NEW THERAPIES

The seriousness and complexity of inflammatory bowel disease (IBD) pose unique challenges to both patients and their physicians, challenges that require highly specialized expertise and a multidisciplinary approach to long-term management and treatment.

The Inflammatory Bowel Disease Program (IBDP) at the University of Michigan is internationally recognized for its team—now 12 faculty strong—that focuses specifically on IBD care and IBD-related scientific, clinical and outcomes research. The program has added seven new faculty members in the past five years alone.

“Expanding the scope of our clinical practice enables us to accommodate more patients and meet the demand from referring physicians,” said **PETER HIGGINS, MD, PhD, MSc**, who directs the program. “Most newly referred patients now can be seen within a week.”

In addition to improved access to physicians, patients—many of whom have not responded to previous treatments—also have access to experimental and cutting-edge therapies. The U-M IBDP is one of the largest IBD clinical trial centers in the world, and patients can be referred by their own doctors directly to the trials. To facilitate referrals to trials, the IBDP recently instituted a simple fax process that mirrors the standard clinic referral process.

Current research includes studies of novel therapies, of how to optimize approved therapies and how to predict which drugs are more likely to work for particular patients in order to personalize care. Clinical trials

of several new anti-inflammatory therapies in the anti-JAK, IL-23, and SMAD-7 pathways are encouraging, and investigators are looking toward next-generation agents that not only control inflammation but could also reverse fibrosis.

In addition, new research tools are being developed to assess the degree of bowel damage to better determine which patients have refractory damage and should consider surgery. A joint clinic between colorectal surgeons and gastroenterologists specializing in IBD is taking that research and using it to help patients and their doctors weigh surgical and non-surgical options. In many cases, the coordination of cutting-edge medical therapy for IBD and

well-timed surgical therapy can reduce the amount of intestine that needs to be removed. This reduces the long-term risk of short gut, a feared complication of poorly controlled IBD. The team, with the patient at the center, develops coordinated treatment plans and can make more informed decisions based on objective predictors of disease progression.

Given the complexity of IBD, patient education is a critical part of disease management. The IBDP recently revamped its patient education materials based on guidance from its patient advisory board. New educational videos and other materials now feature clinicians and patients sharing their perspectives on a variety of specific issues around living with IBD.

“Patients love it,” said Dr. Higgins. “There is a huge learning curve with



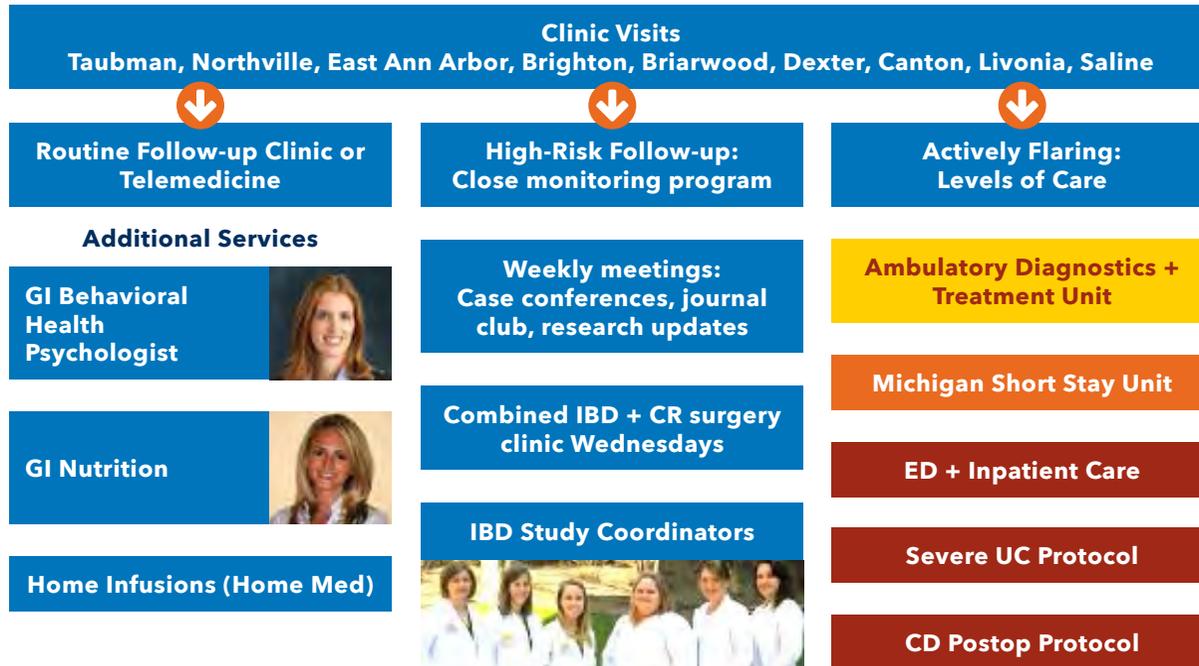
University of Michigan Crohn's and Colitis Team

an IBD diagnosis, and newer patients appreciate learning from experienced patients in addition to their doctor." The program has also created a large and growing series of "IBD School" videos that have been viewed more than 250,000 times on YouTube.

Not only has the IBD program grown in scope; it also has grown in impact. "We are delivering a consistently high level of care to our outpatients and inpatients and reaching more patients throughout Michigan," said Dr. Hig-

gins, "and we're also doing the work that's changing how clinicians all over the world will treat IBD in the future."

As an example, the IBDP recently developed a severe ulcerative colitis protocol based on new evidence and shared it publicly on the web. "Medical centers around the country are using it now," Dr. Higgins added, "and so we're able to have a positive impact on many more patients than we could possibly see in our own program."



**GRACE H. ELTA, MD****ERCP: ENDOSCOPIC THERAPY FOR THE BILIARY AND PANCREATIC DUCTS**

ERCP was first performed as a diagnostic procedure in the late 1970s at the University of Michigan. In 1982, biliary sphincterotomy for stone extraction was added. The field of ERCP in the treatment of pancreatic and biliary disorders grew dramatically after that and now includes pancreatic endotherapy and numerous biliary tract treatments. Examples include biliary manometry, stent placement, intraductal lithotripsy, cholangioscopy, intraductal ultrasound, tissue sampling, stricture dilation, transenteral pseudocyst drainage and necrosectomy. These new treatment modalities significantly reduce the need for invasive surgeries.

## Interventional Endoscopy Program: BEYOND PANCREATIC AND BILIARY CARE

A specialty group within the Division, the University of Michigan Interventional Endoscopy Program (IEP) performs advanced endoscopic procedures to diagnose and treat disorders not only of the pancreas and bile ducts but also the esophagus and colon, and leads clinical research initiatives to continually evolve clinical practice.

The IEP comprises nine faculty: **DRS. AARTI OZA-BEDI, GRACE ELTA, RYAN LAW, JAMES M. SCHEIMAN, ANOOP PRABHU, STACY MENEES, ERIK-JAN WAMSTEKER, RICHARD S. KWON** and **MICHELLE A. ANDERSON**, who serves as physician lead.

The team has led the use of endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP), as well as other complex procedures. The IEP was the first in Michigan to offer EUS and to use it therapeutically.

"The IEP and our patient volumes have grown phenomenally," said **DR. MICHELLE ANDERSON**. "And those high volumes enable ongoing expertise and skill levels that make these complicated procedures safer and more effective for our patients."

### Recognized for excellence in multidisciplinary pancreatitis care and research

The IEP is also the first and to date the only program in Michigan to be designated a National Pancreas Foundation Center of Excellence for acute and chronic pancreatitis.

Through a rigorous auditing process, the IEP was recognized for its high-quality, multidisciplinary care—integrating gastroenterologists, interventional radiologists, surgeons, pain management services and psychosocial support—and advancing research into pancreatitis and related conditions.

Dr. Anderson has led development of national guidelines for the care of patients with painful chronic pancreatitis (*Pancreatology*, 2015; Apr 3: 14(4): 1968-78). Additional research is underway into pain in chronic pancreatitis and EUS. Key findings will inform additional clinical guidelines

for care of inpatients and outpatients with this condition. The aim of the investigations is to decrease emergency department use and readmission, to reduce inpatient length of stay and to improve patients' quality of life.

**DR. JAMES SCHEIMAN**, director of Endoscopic Research and Director of the Advanced Endoscopy Fellowship Program, is working with colleagues in the U-M College of Engineering to develop a sensor technique to determine stent patency. Dr. Scheiman is also involved in ongoing clinical trials to lower the risk of ERCP-induced pancreatitis, which occurs in about 25 percent of patients undergoing the procedure. In work published in the *New England Journal of Medicine* (2012; 366:1414-1422), investigators found that a single prophylactic

dose of indomethacin administered immediately post-procedure can significantly reduce the risk.

### Improving care in pancreatic cancer

Clinicians in the IEP work closely with clinicians in the U-M Comprehensive Cancer Center and recently instituted a clinical protocol for the endoscopic placement of fiducials in pancreatic cancer patients who will undergo radiation therapy. The procedure enables higher and more accurately targeted doses of radiation and helps reduce radiation exposure of surrounding organs and tissues.

To help with pain control in pancreatic cancer, IEP physicians are one of few centers in the state that perform celiac plexus neurolysis.

**DR. STACY MENEES** is studying EUS examination findings in patients with BRCA, an inherited genetic mutation that places patients at risk for both breast and pancreatic cancer. The goal of this project is to identify features that predict risk and to guide screening recommendations. **DR. RICHARD KWON** is using morphomics to conduct risk assessments for patients with cystic neoplasms of the pancreas who are at risk for pancreatic cancer.

### Broadening procedures and treatment options

The IEP clinicians perform interventional endoscopic procedures for a wide range of GI disorders, beyond the pancreatobiliary system. Such procedures include endoscopic mucosal resection and ablation in early

esophageal cancer and in Barrett's Esophagus with dysplasia. The IEP also is one of few places in the state to perform peroral endoscopic myotomy (also known as POEM) for achalasia and intra-operative ERCP through laparoscopic gastrotomy in patients with prior gastric bypass.

One of the added advantages of the IEP at the University of Michigan is the provision of "on-site" pathology at the time of a procedure. This helps ensure adequate samples are obtained, thereby reducing the number of potential procedures and improving the patient experience.

Improved care quality and patient experience are the goals of all IEP clinical and research efforts, and the program is equipped to achieve them.

"With our expertise," said Dr. Anderson, "we're not only able to take care of patients with more complex needs; we're also able to do the research required to continually advance the treatments we can offer them."

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Bioartography.com

**Bryan Stump, DDS**

GOOD COMMUNICATION BRINGS HOPE AND EASIER DECISION-MAKING

**When Bryan Stump, DDS, was diagnosed with pancreatic cancer, his primary care physician referred him to a gastroenterologist at the University of Michigan Medical School. Dr. Stump met with MICHELLE A. ANDERSON, MD, MSc, who, two days later, placed a stent in Dr. Stump's bile duct to relieve some of his symptoms. The blocked duct was impairing drainage of bile, leading to severe itching and jaundice.**

At the same visit, Dr. Anderson performed an endoscopic ultrasound-guided biopsy of the pancreas. When it came back negative for cancer, she called Dr. Stump back to repeat the procedure. That biopsy came back negative as well.

"We were perplexed at first," said Dr. Stump, whose imaging tests had showed masses on his pancreas,

"but Dr. Anderson started giving me hope. 'This could be better than what we were thinking,'" he recalled her saying.

Dr. Anderson had begun to suspect Dr. Stump might have been suffering not from pancreatic cancer but from a rare autoimmune condition called autoimmune pancreatitis. She consulted with colleagues, both at U-M and at other institutions, and she shared her thoughts with Dr. Stump.

If her diagnosis was right, a three-month course of oral steroid medications could resolve the

problem. However, if Dr. Stump did indeed have cancer, three months might mean metastasis to other parts of the body.

"Needless to say, it was a hard decision," said Dr. Stump, "but Dr. Anderson left it up to me entirely. Only after I told her I wanted to try the steroid treatment did she say, 'I'm glad you said that.'"

Both patient and doctor were even gladder about the results. After three months of treatment with steroids, two of the masses had resolved and two others had shrunk dramatically. Liver

enzymes in his blood were approaching normal levels.

Dr. Stump is now symptom- and medication-free. He sees Dr. Anderson just once a year to make sure the masses haven't returned. And he's back to work full time at his dental practice, something he wasn't sure he'd be able to do again.

"It was definitely a life-changing experience, with some big decisions to make," said Dr. Stump, "and I received the best care I've ever gotten. After I saw Dr. Anderson the first time, she and her nurse Terri [Johnson, RN] were in constant contact about test results and other things. I was not left wondering all the time."

Michelle A. Anderson, MD, MSc



# Patient Story



## Cancer Genetics:

DEVELOPING NEW WAYS TO IDENTIFY THOSE AT RISK AND PREVENT COLON CANCER

In the United States, colorectal cancer (CRC) is the third most common type of cancer, although, in the vast majority of cases, it is preventable. In her work as director of the University of Michigan Cancer Genetics Clinic, **ELENA M. STOFFEL, MD, MPH**, focuses on new ways to identify individuals with a genetic predisposition to cancer who may benefit from enhanced screening and surveillance in order to prevent CRC.

The U-M Cancer Genetics Clinic cares for more than 250 families with genetic syndromes associated with increased risk for developing CRC, including familial adenomatous polyposis (FAP) and Lynch syndrome, also known as hereditary non-polyposis colorectal cancer. Through the clinic, Dr. Stoffel and her team coordinate genetic testing to identify individuals who have increased risk for cancer. She and her team also coordinate clinical trials to investigate the effectiveness of screening tests and medications for preventing cancers from developing in patients whose

lifetime cancer risk exceeds 70 percent without intervention.

The GI Division has a long, illustrious history of pioneering colon cancer research. In 1995, **DR. RICHARD BOLAND** uncovered the role of DNA mismatch repair in regulating the G2/s cell cycle checkpoint, and the prediction that colon cancer with microsatellite instability would be resistant to chemotherapy. This set the foundation for subsequent studies on colon cancer genetics.

The laboratory of **JOHN M. CARETHERS, MD**, Chair of the

Department of Internal Medicine, studies the pathogenesis of sporadic and hereditary colorectal cancer. The laboratory focuses on the function and



John Carethers, MD

consequences of the DNA mismatch repair system which when affected, is involved in both inherited and sporadic colorectal cancer. His lab seeks to understand the basic mechanisms of DNA mismatch repair in human cells and investigates the role of inflammation and DNA mismatch repair regulation. His laboratory has identified that colorectal cancers exhibiting increased inflammatory cells showcase a biomarker called EMAST, which appears to be caused by MSH3 (DNA mismatch repair gene) dysfunction. In addition, Dr. Carethers' laboratory strives to understand possible biological differences and possible approaches to the racial disparity seen in the morbidity and mortality from colorectal cancer. This series of work has elucidated the pathogenesis of sporadic and hereditary colorectal

cancer and provides potential preventative and/or therapeutic targets.

Current clinical studies include trials of chemopreventive agents, including nonsteroidal anti-inflammatory drugs, to slow the growth of polyps. **DRS. TOM WANG** and **KIM TURGEON** are investigating ways to use novel endoscopic technologies to better visualize the colon and identify polyps, since—particularly in Lynch syndrome—precancerous polyps can be small, flat and hard to discern.

“What we’ve found in our work is that the initial clinical criteria and algorithms used in risk assessment are not sufficiently sensitive to identify everyone who is at risk of colon cancer,” said Dr. Stoffel. “We want to devise better ways for patients at risk to be identified by their primary care



Kim Turgeon, MD

physicians and gastroenterologists before they develop colorectal cancer.”

In fact, many CRC patients who are found to carry mutations associated with hereditary cancer syndromes don’t meet the typical family history criteria. One in three patients diagnosed with FAP is the first in their family to develop CRC. Preliminary data from analyses

Dr. Stoffel has conducted, presented as an abstract at Digestive Disease Week 2016, suggest that one in five patients under 50 diagnosed with CRC may have an inherited mutation in known cancer susceptibility genes, including those that cause Lynch syndrome, FAP and other less common syndromes.

“There is a pressing need to find new ways to identify these people earlier that don’t rely on family history,” said Dr. Stoffel.

In related work, Dr. Stoffel is also interested in better understanding the rising incidence of colon cancer in young people and racial disparities in incidence and survival. “While colorectal cancer incidence is decreasing overall, it’s on the rise in younger patients, and we’re also seeing racial disparities in outcomes that we think

may be related to characteristics of tumor biology, rather than disparities in screening, medical care or comorbid conditions”

Using data from SEER (Surveillance, Epidemiology and End Results), Dr. Stoffel analyzed outcomes for CRC patients under 50, and found the survival rate for blacks was lower at every stage of the disease and particularly striking among individuals with stage II cancers.

“We’re hypothesizing that tumors in young people under 50 are probably different than those in older people, and there also may be differences by race in tumor characteristics that contribute to racial disparities in CRC outcomes,” said Dr. Stoffel.

The findings have important implications for treatment, since the benefits

of chemotherapy in stage II CRC has been a topic of debate, Dr. Stoffel noted. “And it may be that tumors in young people are more aggressive, and the chemotherapy we use in older patients may or may not be adequate for treating the young.”

Further work will investigate molecular characteristics of tumors in CRC patients under 50 to better understand why and how the disease develops.

The continued findings from Dr. Stoffel’s work will no doubt inform how patients at risk of cancer are identified, screened and cared for. “Taking care of families that have these inherited mutations and knowing that in the younger generations we can intervene to prevent cancer is incredibly motivating,” she said.

## Esophageal Disorders Program

ADVANCING RESEARCH, ADVANCING CARE

With more than a dozen faculty, the University of Michigan Esophageal Disorders Program (EDP) continues to offer patients new treatment approaches based on discoveries generated through its ongoing clinical research efforts.

The EDP treats both routine and complex disorders, including achalasia, Barrett's Esophagus, swallowing problems, eosinophilic esophagitis, esophageal cancer and symptoms of gastroesophageal reflux disease refractory to acid-reducing medications.

### Diagnosing and managing motility-related disorders

To define etiology and guide treatment of motility-related issues, the EDP is one of only a very few centers in the region with physicians experienced in the use of EndoFLIP® (Endolumenal Functional Lumen Imaging Probe), to measure esophageal distensibility during endoscopy, which provides complementary infor-

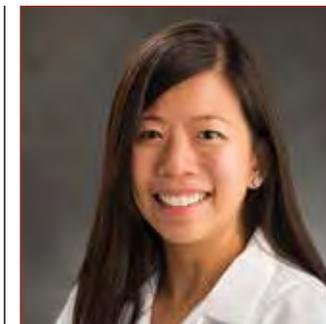
mation to manometry. Therapeutically, EndoFLIP can be used for dilation, eliminating the radiation exposure associated with the conventional fluoroscopic method.

The treatment of esophageal motility-related disorders has also evolved. The EDP offers peroral endoscopic myotomy (POEM) for the treatment of achalasia and other spastic esophageal disorders. This procedure, led by **DR. RYAN LAW**, is analogous to the surgical gold standard, laparoscopic Heller myotomy. This endoscopic procedure involves the creation of a tunnel within the esophageal wall followed by electroincision of the circular muscle,

thereby improving food passage from the esophagus to the stomach.

### Research drives care

Several investigations are informing care for motility-related disorders. For the past 18 months, the EDP has been gathering questionnaires about symptom severity from patients undergoing esophageal manometry and reflux testing. Given the high volume of procedures—746 and 481, respectively, in 2015—the data are facilitating several studies led by **JOAN CHEN, MD, MSc**, including esophagogastric junction outflow obstruction (EGJOO) and how to discern when the diagnosis is clinically relevant and warrants intervention.



Joan Chen, MD, MSc

For eosinophilic esophagitis (EoE), the EDP is one of several clinical sites conducting a Phase 3 randomized controlled trial of oral budesonide solution. If approved, it would be the first EoE treatment to receive FDA approval.

In close collaboration with allergists and dietitians, the EDP has developed a 4-food empirical food elimination

protocol for the most common food allergies in EoE patients. And data from a new registry of EoE patients dating back to 2000 in conjunction with validated survey instruments are being used in studies to compare treatment outcomes.

In fact, the EDP has established registries for a number of esophageal disorders in addition to EoE, including dysmotility, reflux and Barrett's Esophagus.

"These registries help us develop observational studies and other research that will enable development of interventional investigations," said **JOEL RUBENSTEIN, MD, MSc**, who directs the Barrett's Esophagus Program within the EDP. "Registries provide a wealth of information that we then use to develop and test hypotheses."



Joel Rubenstein, MD, MSc

### Barrett's Esophagus investigations

The registry of Barrett's Esophagus includes nearly 3,000 patients, and has led to a study looking at the natural history of Barrett's Esophagus with low-grade dysplasia that was presented in a lecture at Digestive Disease Week in May 2016. The findings showed

a much higher risk of progression to cancer—on the order of 3 percent per year—than among earlier U.S. cohorts. The risk was previously believed to be about tenfold lower.

Other research includes studies of surveillance quality in Barrett's Esophagus patients to identify potential over- and/or underutilization of endoscopy over the past 20 years. In a first-of-its-kind study, EDP investigators also are looking at quality of life in Barrett's patients who underwent endoscopic therapy for neoplasia versus controls who underwent esophagectomy.

Through the Barrett's Esophagus Translational Research Network (BETRNet), **THOMAS WANG, MD, PhD** and Professor of Surgery **DAVID BEER, PHD**, have developed novel peptide sprays that specifically bind to

neoplastic cells. The probes are used during fluorescent endoscopy, an imaging method developed at U-M by Dr. Wang. Clinical trials will begin shortly. This network of academic institutions combines scientific expertise across diverse campuses to develop new methods for early detection of esophageal cancer. Early biological events that drive cancer transformation, improve our understanding of the role of precursor lesions and lead to more effective cancer surveillance methods. NIH has provided U-M with more than \$6 million in funding over the past five years to support this effort.

The EDP also has been a leader in helping primary care physicians diagnose Barrett's Esophagus in certain patient groups using the Michigan Barrett's Esophagus pREdiction Tool (M-BERET).

The tool was developed from the Newly Diagnosed Barrett's Esophagus Study conducted at U-M and the Ann Arbor Veterans Affairs Medical Center (*American Journal of Gastroenterology*, 2013; 108(3): 353-362). A grant from the Department of Veterans Affairs is supporting validation of the tool in additional patient groups.

In summary, we have a comprehensive Esophageal Disorders Program. Our robust research programs are supported by federal funding which drives our state-of-the-art clinical care.



Thomas Wang, MD, PhD

## Ann Arbor VA Healthcare System: LEVERAGING TECHNOLOGY TO IMPROVE ACCESS, CARE AND OUTCOMES

Finding novel ways to deliver care is a hallmark of the UM-affiliated VA Ann Arbor Healthcare System (VAAAHS). Staffed by University of Michigan Medical School faculty, the VAAAHS is intrinsically driven by the same three-part mission: clinical care, education and research, including basic, clinical and health services investigations.



Grace Su, MD

As the country's largest integrated health system, the veterans' health-care system was also one of the first

to implement electronic medical records (EMR).

"This EMR system is an incredible resource for both patients and physicians that can be harnessed for innovative research and for creating new approaches to patient care," said **GRACE SU, MD**, chief of the VAAAHS Gastroenterology Section and associate chief of medicine for subspecialty care and access.

### **Improving access to subspecialty care and distance learning**

Dr. Su led the development of, and now directs, a transformational program dubbed SCAN-ECHO (Specialty Care

Access Network–Extension of Community Healthcare Outcomes). The goal of the virtual program is to improve subspecialty care delivery within the VA healthcare system, particularly for veterans and primary care providers in underserved and rural areas.

The SCAN-ECHO program, funded through a Veterans Health Administration (VHA) Healthcare Transformation Initiative (T21) grant, incorporates both real-time case consultations among remote primary care physicians and U-M Gastroenterology and Hepatology specialists. The program includes

a distance learning component, with educational sessions for which physicians can earn continuing education credit.

“Over time, by sharing treatment strategies for specific cases and discussing new medical research, the primary care physicians and specialists at the VAAHS develop close working relationships, which only improves care for patients,” said Dr. Su.

“Since the VAAHS serves as a tertiary care referral center for other VA health systems within a wide region, including Michigan, Indiana and much of Ohio, a program like this saves many patients from costly and inconvenient travel as they can be treated in their own communities,” Dr. Su added.

About two-thirds of patients referred to the VAAHS liver clinic are patients outside the system’s catchment area and, on average, patients travel 160 miles roundtrip to be seen in Ann Arbor.

For primary care physicians in remote and underserved areas, the program enables them to diagnose, treat and manage patients with more complex chronic diseases, gaining valuable insight and expanding their expertise.

The Ann Arbor SCAN-ECHO program is one of the largest—and one of the first—to focus specifically on hepatology subspecialty care for veterans. A recent study published by Dr. Su and colleagues in the *American Journal of Gastroenterology* (2016; 111(6):838-44) found that, for patients with liver

disease, access to specialty care was associated with an improved five-year survival rate. The findings support the need for innovative use of technology to expand access to subspecialists.

#### **Screening and treating hepatitis C and other liver diseases—virtually**

In addition to SCAN-ECHO, the VAAHS uses other electronic and virtual care delivery models. By looking at EMR data and patient registries, the health system can identify and reach out to patients with diagnosed but untreated liver disease, linking them to much-needed care.

Patients with liver disease may be managed through community-based outpatient clinics in Jackson, Flint and Toledo by physicians trained by U-M specialists. Other patients may opt for

virtual and telemedicine approaches, depending on their location and condition.

“We always let patients know we can still help, even if travel is difficult for them,” said Dr. Su. “It might mean they have to come to Ann Arbor once for an initial visit, but now we can offer them several options for their long-term care and management.”

#### **Assessing risk and improving outcomes through morphomics**

The VAAHS’ vast repository of data supports another innovative approach to health services research and care delivery—the use of analytic morphomics to assess a patient’s current condition, identify risk factors and tailor treatment.

Through groundbreaking analyses, Dr. Su and colleagues have shown that a number of biomarkers derived from imaging provide quantifiable insights into a patient’s state (publication citations available at [med.umich.edu/surgery/morphomics](http://med.umich.edu/surgery/morphomics)). Those biomarkers include organ size and condition; volume and quality of particular muscles and muscle groups; visceral and subcutaneous fat volumes, distribution and density; bone shape; and certain vascular measures. Using morphomics, physician investigators are able to predict cirrhosis and determine the best treatment option for patients who go on to develop liver cancer.

Morphomics efforts are currently underway to assess disease activity and progression in liver, pancreatic, inflammatory bowel and Crohn’s disease in



order to personalize patient treatments and improve outcomes.

"The beauty of morphomics within such a large, integrated system as the VAAAHS is that it accurately quantifies information we already have in patients' electronic records from imaging and combines it with other clinical data," said Dr. Su, who serves as associate director for the University of Michigan Morphomics Analysis Group. "We're putting the data to work in order to figure out how best to personalize care for each patient."

**Predicting esophageal adenocarcinoma in patients with Barrett's Esophagus**

**JOEL RUBENSTEIN, MD, MSc**, has developed the Michigan Barrett's Esophagus pREdiction Tool (M-BE-



Joel Rubenstein, MD, MSc

RET), a pre-clinical tool to predict whether a patient has Barrett's Esophagus ([mberet.umms.med.umich.edu](http://mberet.umms.med.umich.edu)). It uses only a few simple questions about symptoms of gastro-esophageal reflux and tobacco use, as well as measurements of waist and hip circumference.

Ann Arbor VA Hospital

Dr. Rubenstein has received a grant from the Department of Veterans Affairs to validate the accuracy of the tool in a population of 1,500 patients undergoing their first upper endoscopy. He will also retrospectively apply it to a population of 100,000 individuals who have that data available from the late 1960s and were followed longitudinally since then. The aim is to determine whether the tool accurately predicts which of those individuals developed esophageal adenocarcinoma.

#### **Optimizing selection of patients for colon cancer screening**

**SAMEER SAINI, MD, MSc**, uses computer microsimulation modeling to estimate the benefits and harms of colorectal cancer screening for



Sameer Saini, MD, MSc

individual patients. These estimates can be used to help physicians make more individualized decisions about cancer prevention. The estimates can also be presented to patients who are considering screening, allowing them to make more informed decisions about their health. By implementing these data into clinical practice,

clinicians can ensure that patients who are likely to benefit get screened, and those who are not likely to benefit avoid unnecessary and costly care.

#### **Personalizing treatment for IBD**

**AKBAR WALJEE, MD, MSc**, also uses computers and predictive models to provide better decision-making for tailored and individualized care, especially in costly GI diseases and low-resource settings. Dr. Waljee has been working with colleague **DR. RYAN STIDHAM** to develop new tools using analytic morphomics to measure disease severity in Crohn's patients. Using machine learning, Dr. Waljee integrates the information from imaging studies with laboratory and medical data available in patient electronic medical records to develop better



Akbar Waljee, MD, MSc

decision support tools for physicians to individualize treatments for patients with inflammatory bowel disease.

#### **Growth offers educational opportunities**

The novel approaches to delivering specialized gastroenterology and

hepatology care at the VAAHS create a fertile training ground for the next generation of physicians.



# **Education + Training**

## Fellows

Training the next generation of gastroenterologists and hepatologists is the primary mission of the Division. The University of Michigan is recognized both for its excellent clinical training as well as for its top ranked training in basic science, outcomes and health services research. During the last 75 years, the Division has trained more than 400 gastroenterologists and hepatologists who are practicing in 33 states. Many of our trainees have evolved into outstanding clinicians, clinical leaders and academic leaders in their own right.

### Gastroenterology Fellows 1st Year

**Dennis Chen**, 2016-2019  
**Vincent Chen**, 2016-2019  
**Amar Mandalia**, 2016-2019  
**Chanakyaram Reddy**, 2016-2019  
**Arjun Sondhi**, 2016-2019  
**Mary Thomson**, 2016-2019  
**Dabo Xu**, 2016-2019

### Gastroenterology Fellows 2nd Year

**Joy Chang**, 2015-2018  
**Phillip Chisholm**, 2015-2018  
**Anand Patel**, 2015-2018

**Arpan Patel**, 2015-2018  
**Shreya Sengupta**, 2015-2018  
**Eric Shah**, 2015-2018  
**Matthew Sturm**, 2015-2018

### Gastroenterology Fellows 3rd Year

**Paul Corsello**, 2014-2017  
**Anand Jain**, 2014-2017  
**Tossapol Kerdsirichairat**, 2014-2017  
**Jenny Maratt**, 2014-2017  
**Marc Piper**, 2014-2017  
**Anna Tavakkoli**, 2014-2017  
**Andy Wright**, 2014-2017

### Transplant Hepatology Fellows

**Rinjal Brahmbhatt**, 2016-2017  
**Dekey Lhewa**, 2016-2017

### Advanced Endoscopy Fellows

**Amy Hosmer**, 2016-2017  
**Dmitry Shuster**, 2016-2017

### Fellows 1954-2016

**Basil Hirschowitz**, 1954  
**Donald Kuiper**, 1969  
**Bergein Overholt**, 1969  
**Newell Augor**, 1970  
**Eugenius Ang**, 1971  
**Haair Aharonian**, 1975

**Mohammed Farivar**, 1975  
**Eugene Rudolph**, 1975  
**Harold Tobes**, 1975  
**Charles Balabaud**, 1976  
**Daniel Biery**, 1976  
**Berj Minasakanian**, 1976  
**Peter Naus**, 1976  
**Varin Uppaputhangkule**, 1976  
**Alan C. Dopp**, 1977  
**Peter Hooberman**, 1977  
**Roberto Prizont**, 1977  
**Sai Sista**, 1977  
**John S. Farrell**, 1978  
**Safiul Hasan**, 1978  
**Hossein Tavassollie**, 1978  
**Joel V. Weinstock**, 1978  
**Nefins Barlas**, 1979  
**Mostafa Ibrahim**, 1979  
**Timothy Nostrant**, 1979  
**John A. Schaffner**, 1979  
**Hidenori Kawanishi**, 1980  
**Manus Krasman**, 1980

**Jean-Pierre Raufman**, 1980  
**Sami Achem**, 1981  
**Patricia Sell**, 1981  
**Charles Thueson**, 1981  
**Ferdinand Balatico**, 1982  
**Joseph Davanzo**, 1982  
**Patricia Kuzma Sell**, 1982  
**Gary Monash**, 1982  
**Herman Perman**, 1982  
**Michael Persaud**, 1982  
**Joseph Tan**, 1982  
**Howard Wallace**, 1982  
**Robert Winchell**, 1982  
**Edward Clay**, 1983  
**Paul Giradi**, 1983  
**Gary Hills**, 1983  
**Brian Liska**, 1983  
**John Joseph Wells**, 1983  
**Thomas Huber**, 1984  
**Patricia Lorusso**, 1984  
**Baldev Malik**, 1984  
**Milton Mutchnick**, 1984

**Allan Coates**, 1985  
**Arthur French**, 1985  
**Bruce Kovan**, 1985  
**John Persson**, 1985  
**Joyce Richards**, 1985  
**Jeffrey Sams**, 1985  
**John Del Valle**, 1986  
**Gary Falk**, 1986  
**Daniel Fall**, 1986  
**William Gracie**, 1986  
**Robert Helft**, 1986  
**Russell Keinath**, 1986  
**H. Horchang Lee**, 1986  
**Wilfred Lee**, 1986  
**Stanley Strasius**, 1986  
**JoAnne Wilson**, 1986  
**Rex Antinozzi**, 1987  
**Jeffrey Barnett**, 1987  
**Jian-Jun Chen**, 1987  
**Michael Lucey**, 1987  
**Joel Montbriand**, 1987  
**Robert Rose**, 1987

**James Scheiman**, 1987  
**Peter Traber**, 1987  
**William Weatherhead**, 1987  
**Andrew Welch**, 1987  
**John Wiley**, 1987  
**Friedrich Loura**, 1988  
**Chester Zahn**, 1988  
**Leslie Aldrich**, 1989  
**Tom Colturi**, 1989  
**William Hasler**, 1989  
**James Vanpopering**, 1989  
**Peter Walsh**, 1989  
**Dale Bachwich**, 1990  
**W. Michael McDonnell**, 1990  
**Gustavo Torres-Barrera**, 1990  
**Danielle Turgeon**, 1990  
**Ellen Zimmerman**, 1990  
**Daryl Daugherty**, 1991  
**John Farnen**, 1991  
**Steve Kuehn**, 1991  
**James H. Morse**, 1991  
**Pat Mortell**, 1991

**Rosanne Murphy**, 1991  
**Bahri Bilir**, 1992  
**Kim Brown**, 1992  
**William Dobbins**, 1992  
**Ken Lown**, 1992  
**Arnold Markowitz**, 1992  
**David Roberts**, 1992  
**Andrea Todisco**, 1992  
**Traver Traber**, 1992  
**Gary Wu**, 1992  
**Nuray Bilir**, 1993  
**William Chey**, 1993  
**Michael Kochman**, 1993  
**Stephen Kuehn**, 1993  
**Steven Taylor**, 1993  
**John W. Walsh**, 1993  
**Caryn Berkowitz**, 1994  
**Laurel Fisher**, 1994  
**Joseph Henderson**, 1994  
**Tom Judge**, 1994  
**Ken Kohagen**, 1994  
**Mark Sims**, 1994

**Khalouck Abdrabbo**, 1995  
**Rajiv Bansal**, 1995  
**John Carethers**, 1995  
**Robert Fontana**, 1995  
**William Grady**, 1995  
**Graeme MacDonald**, 1995  
**Donn Marutani**, 1995  
**Frederick Askari**, 1996  
**Gyorgy Baffy**, 1996  
**Cary Caldwell**, 1996  
**Steve Carpenter**, 1996  
**Robert Holmes**, 1996  
**Srinivas Janardan**, 1996  
**Joseph Kolars**, 1996  
**Eric Mortensen**, 1996  
**Stephen Webster**, 1996  
**Sherin Koshy**, 1997  
**Mimi Takami**, 1997  
**William Tierney**, 1997  
**Richard T. Wille**, 1997  
**Michael Yeh**, 1997  
**Michael Cannon**, 1998

**Naresh Gunaratnam**, 1998  
**Mark Jeffries**, 1998  
**Margaret Kinnard**, 1998  
**Steven Klein**, 1998  
**Uri Ladabaum**, 1998  
**Robert O'Shea**, 1998  
**Michelle Anderson**, 1999  
**Byunki Kim**, 1999  
**Partha Nandi**, 1999  
**Shanthi Srinivasan**, 1999  
**Mark Stern**, 1999  
**Adam Gorelick**, 2000  
**Khazema Hussain**, 2000  
**Ernest Ofori-Darko**, 2000  
**Melissa Rich**, 2000  
**Ezra Burstein**, 2001  
**Manish Chokshi**, 2001  
**Matthew DiMugno**, 2001  
**Kelvin Hornbuckle**, 2001  
**John C. Rabine**, 2001  
**John Kao**, 2002  
**Mark Marilley**, 2002

**Kimya Nguyen**, 2002  
**Leonard Quallich III**, 2002  
**Thomas Shehab**, 2002  
**Erik-Jan Wamsteker**, 2002  
**Ali Yazdani**, 2002  
**Betty Kim**, 2003  
**James Rhee**, 2003  
**Krishnavel Chathadi**, 2004  
**Peter Higgins**, 2004  
**Mary Ann Huang**, 2004  
**Jason Phillips**, 2004  
**Cyrus Piraka**, 2004  
**Joel Rubenstein**, 2004  
**Ahmed Sherif**, 2004  
**Michael Cleary**, 2005  
**Luke Evans**, 2005  
**Dave McMillen**, 2005  
**Stacy Menees**, 2005  
**Richard J. Saad**, 2005  
**Agata Bednarz**, 2006  
**Taft Bhuket**, 2006  
**Stephen Brackbill**, 2006

**Wei Ming Sun**, 2006  
**Hellan Kang**, 2007  
**Chun Hsu**, 2007  
**Nonthalee Pausawasdi**, 2007  
**Ryan Taylor**, 2007  
**Michael Volk**, 2007  
**Mark Zeglis**, 2007  
**Haritha Avula**, 2008  
**Badih Elmunzer**, 2008  
**Darren Brenner**, 2008  
**Syed Abbas Fehmi**, 2008  
**Robert Pompa**, 2008  
**Sameer Saini**, 2008  
**Pratima Sharma**, 2008  
**Dahlia Awais**, 2009  
**Amaar Ghazale**, 2009  
**Soojong Hong**, 2009  
**Vinay Katukuri**, 2009  
**Aparna Repaka**, 2009  
**Akbar Waljee**, 2009  
**Craig Womeldorph**, 2009  
**Nicholas Boetticher**, 2010

**April Grudell**, 2010  
**Akshay Gupta**, 2010  
**Mohammed Jafri**, 2010  
**Nirmal Kaur**, 2010  
**Niloy Jewel Samadder**, 2010  
**Amit Singal**, 2010  
**Jason Taylor**, 2010  
**Constantinos Anastassiades**, 2011  
**John Bassett**, 2011  
**Jason Lewis**, 2011  
**Rajnish Mishra**, 2011  
**Michael Rajala**, 2011  
**Ryan Stidham**, 2011  
**Shannan Tujios**, 2011  
**Julie Yang**, 2011  
**Eugene Zolotarevsky**, 2011  
**William Cooney**, 2012  
**Sharlene D'Souza**, 2012  
**Jennifer Jorgensen**, 2012  
**Beth Manoogian**, 2012  
**Michelle Muza-Moons**, 2012  
**Darashana Punglia**, 2012

**Mina Rakoski**, 2012  
**Amol Rangnekar**, 2012  
**Steven Scaglione**, 2012  
**Benjamin Young**, 2012  
**Nisa Kubiliun**, 2013  
**Joshua Max**, 2013  
**Diane Nguyen**, 2013  
**Aarti Oza Bedi**, 2013  
**Anoop Prabhu**, 2013  
**Reena Salgia**, 2013  
**Heather Simpson**, 2013  
**Yu-Ming Chang**, 2014  
**Neel Choksi**, 2014  
**Radoslav Coleski**, 2014  
**Anthony DeBenedet**, 2014  
**Shail Govani**, 2014  
**Bari Khurram**, 2014  
**Megan Adams**, 2015  
**Tannaz Guivatchian**, 2015  
**Jacob Kurlander**, 2015  
**Robert Lapp**, 2015  
**Sean McCarthy**, 2015

**Jessica Mellinger**, 2015  
**Andrew Reinink**, 2015  
**Andrew Shreiner**, 2015  
**Graham Brady**, 2016  
**Alison Freeman**, 2016  
**Amy Hosmer**, 2016  
**Monica Konerman**, 2016  
**Alexander Larson**, 2016  
**Andrew Nett**, 2016  
**Pranith Perera**, 2016  
**Andrew Read**, 2016  
**Dmitry Shuster**, 2016  
**Marisa Spencer**, 2016  
**Erin Spengler**, 2016



Hari Conjeevaram, MD, MSc

## University of Michigan Gastroenterology Fellowship Program: EDUCATING THE LEADERS AND BEST

One of the largest and most highly respected gastroenterology training programs in the United States, the University of Michigan Gastroenterology Fellowship Program is recognized both for its clinical training as well as for its top-ranked training in basic science and outcomes research.

"The volume of procedures, exposure to a breadth of experts in many subspecialty areas, myriad cutting-edge clinical and outcomes research opportunities and many other factors make the three-year U-M GI Fellowship Program truly stand out," said **HARI CONJEEVARAM, MD, MSc**, Professor of Medicine, Division of Gastroenterology and Hepatology and director of the fellowship program since September 2010.

### Individualized training

Fellows' interests, skills, educational goals and passions all drive an individualized fellowship experience.

Beyond meeting Accreditation Council for Graduate Medical Education training requirements, the U-M Gastroenterology Fellowship Program offers additional, integrated training via several novel programs:

- National Clinician Scholars Program
- Graduate Medical Education Scholars Program
- House Staff Innovation & Entrepreneurship Program, begun in 2015
- Physician Scientist Training Program (NIH T32 DK094775)

- Master of Science degree in Clinical Research Design and Statistical Analysis through the U-M School of Public Health (NIH T32 DK062708)
- Forthcoming business and leadership training program, leading to a Master of Business Administration degree

### Support, mentorship and collaboration

The U-M Gastroenterology Fellowship Program is one of the only GI training programs funded with the support of two highly competitive

National Institutes of Health (NIH) Training Grants, one in Basic Science Research Training and a second in GI Epidemiology. The U-M Training Program in GI Epidemiology is one of only three such outcomes research training programs in the country.

Currently, the U-M GI fellowship program has been able to support at least two fellows through the National Clinician Scholars Program. The NIH Basic Science and Translational Research Training Grant provides funds to train up to three GI fellows interested in basic and translational digestive sciences. The NIH GI Epidemiology and Outcomes Training grant which support two GI fellows focuses on clinical outcomes and investigation with resources and tools commonly utilized, including large

databases, cost-effective analysis, meta-analysis and other health services research techniques.

"The amount of support that our fellows receive in clinical and research training, in mentorship from faculty and through a high degree of collaboration with other departments and schools within the University affords our trainees a truly unique fellowship experience," said Dr. Conjeevaram.

### **Demonstrating excellence and supporting success**

The U-M Gastroenterology Fellowship Program currently has 21 fellows (seven per year), among the largest programs in the nation. Graduates are highly sought for advanced fellowship training, for example in Advanced Hepatology or Advanced Endoscopy,

and recruited for faculty positions in other academic institutions as well as private practice settings. In the past few years, 80 to 100 percent of graduating fellows have stayed in academia.

Fellows' accomplishments reflect the dedication and investment of GI division faculty and mentors in integrated programs as well as the personalized approach.

"We work hard to bring out the best in our trainees by allowing them to find their individual passions in the field, to think and to be creative," said Dr. Conjeevaram, "and we provide them with the best environment we can and the resources they need to find their niche and achieve their potential."



## Training Gastroenterologists to Perform Clinical and Outcomes Research:

### THE NEXT STEP

Scientific discoveries in the laboratory are most helpful when findings are translated, through clinical trials, into new therapies and diagnostic tools. But developing new therapies and diagnostic tools is not enough—physicians also need to deliver these services to the right patients at the right time, ensuring timely and high-quality care. As the U.S. healthcare system changes, there is a greater focus on quality of care as opposed to quantity of care, and outcomes and health services research informs the delivery of optimal clinical care. Such research also aids in the development of clinical practice guidelines and healthcare policy.

The Division of Gastroenterology and Hepatology is home to the Training Program in GI Epidemiology, which has been funded continuously by a National Institutes of Health T32 training grant since 2002.

"The performance of clinical trials and research on healthcare delivery is critical to improving patient care, and the first step in that process is to train GI fellows to become GI outcomes researchers," said **PHILIP SCHOENFELD, MD, MEd, MSc (EPI)**, who was director of the program (one

of the few such programs in the nation) from its inception until 2016.



Philip Schoenfeld, MD, MEd, MSc (EPI)

of the few such programs in the nation) from its inception until 2016. During their fellowship, postdoctoral trainees focus on a specific research question, such as quality improvement in colorectal cancer screening with colonoscopy, and complete three core projects: a systematic review, a secondary data analysis and a prospective study under the guidance of a team of mentors.

In order to complete these projects, fellows need formal training. The U-M is fortunate to be able to offer two options: an MS degree in Health Care Policy through the Institute for

Healthcare Policy and Innovation or an MSc degree in Clinical Research Design and Statistical Analysis from the School of Public Health. These programs focus on outcomes research/healthcare policy and clinical trial design, respectively. Both programs provide instruction in statistics and clinical research.

Trainees can also draw upon myriad resources offered at U-M. In addition to the faculty in the Division of Gastroenterology and Hepatology, training program faculty include biostatisticians, healthcare policy experts and experts in clinical trial design and outcomes research. These mentors span, and offer access to resources within the School of Public Health, the Division of General Internal Medicine, the VA Center for Clinical Management Research (a nationally recognized VA Health Services

Research and Development Center of Innovation) and specialized centers within the Institute for Healthcare Policy and Innovation (IHPI).

"With such a breadth of faculty, both within our Division and across the University, our trainees can find content mentors who are experts in virtually any GI topic while also receiving support from methodological mentors across a variety of disciplines," said **SAMEER SAINI, MD, MSc**, who was promoted to Director of the program in 2016 after having served as Associate Director from 2013-2016.

In addition to supporting advanced research training for selected fellows, faculty also support the research education of our GI fellows at large.



Sameer Saini, MD, MSc

Since 2013, Dr. Saini has led the GI Clinical Research Conference, a monthly conference for fellows where ongoing research is presented and discussed in an interactive format. In 2016, Dr. Saini was awarded the Fellows Teaching Award for his role in leading the conference series.

Dr. Saini also is leading efforts to develop a mentoring program for junior faculty interested in GI health services research careers. As Director of the Junior Faculty to K Award (JF2K) Program, he is leveraging Division and Internal Medicine department resources and the infrastructure of the IHPI to build an efficient pathway to career development funding, crucial to junior faculty for securing protected research time and funding additional training. The JF2K Program, in its first year, will serve as a model for other medicine subspecialties developing health services research programs.

"Our goal is to excite GI fellows about clinical, outcomes and health services research and guide them into successful academic careers with independent funding," said Dr. Saini.

The Training Program in GI Epidemiology has a proven track record. Recent trainees include **MEGAN ADAMS, MD, JD, MSc**, a GI health services researcher and attorney with a particular interest in healthcare policy. Dr. Adams, whose work focuses on factors driving use of monitored anesthesia care, was recently appointed Chair-Elect of the AGA Quality Measures Committee. In this role, she will have the opportunity to shape the direction of quality measure development in gastroenterology and work with payers and policymakers on matters related to quality of care.

Other recent graduates include **SHAIL GOVANI, MD, MSc**, an inflammatory bowel disease (IBD) specialist who is examining ways

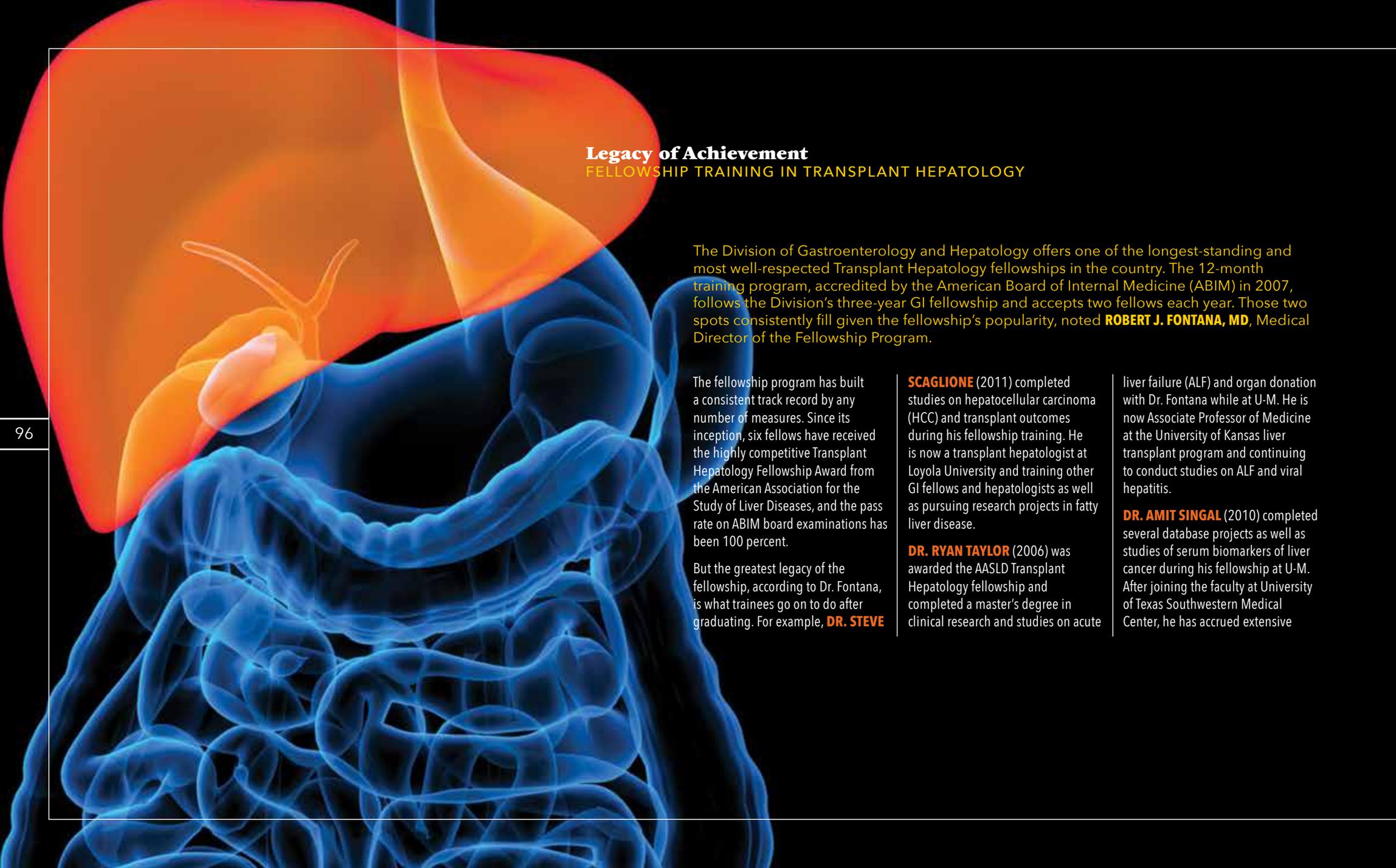
to improve adherence to biologic agents in IBD patients, and **JESSICA MELLINGER, MD, MSc**, a transplant hepatologist with an interest in improving outcomes in patients with alcoholic liver disease.

"Our former trainees are now leaders in GI outcomes and health services research and mentors in their own right, fostering the growth of the next generation of researchers who will develop new approaches to patient care while revising clinical practice guidelines and reshaping healthcare policy," said Dr. Saini.

## PROGRAM SUCCESS AT-A-GLANCE

**Fourteen** GI fellows have completed the program since the first trainees graduated in 2004. Among them,

- **Eleven** are faculty in academic programs that offer gastroenterology fellowship programs.
- **Seven** serve on the faculty at the University of Michigan.
- **Four** of the first five graduates hold the rank of Associate Professor of Medicine with tenure.
- Nine have successfully applied for Career Development Awards from NIH, VA, AASLD and AGA.
- **Seven** have completed their Career Development Award funding, and these physicians are principal investigators on a total of three RO1s, three VA Merit Awards and two large U.S. Department of Defense grants, as well as multiple small federal grants for pilot research.
- Graduates have numerous first-author publications in top journals for clinical and outcomes research, including the *New England Journal of Medicine*, *JAMA*, *BMJ*, *Gastroenterology*, *American Journal of Gastroenterology*, *Gut* and *Hepatology*.



## Legacy of Achievement

### FELLOWSHIP TRAINING IN TRANSPLANT HEPATOLOGY

The Division of Gastroenterology and Hepatology offers one of the longest-standing and most well-respected Transplant Hepatology fellowships in the country. The 12-month training program, accredited by the American Board of Internal Medicine (ABIM) in 2007, follows the Division's three-year GI fellowship and accepts two fellows each year. Those two spots consistently fill given the fellowship's popularity, noted **ROBERT J. FONTANA, MD**, Medical Director of the Fellowship Program.

The fellowship program has built a consistent track record by any number of measures. Since its inception, six fellows have received the highly competitive Transplant Hepatology Fellowship Award from the American Association for the Study of Liver Diseases, and the pass rate on ABIM board examinations has been 100 percent.

But the greatest legacy of the fellowship, according to Dr. Fontana, is what trainees go on to do after graduating. For example, **DR. STEVE**

**SCAGLIONE** (2011) completed studies on hepatocellular carcinoma (HCC) and transplant outcomes during his fellowship training. He is now a transplant hepatologist at Loyola University and training other GI fellows and hepatologists as well as pursuing research projects in fatty liver disease.

**DR. RYAN TAYLOR** (2006) was awarded the AASLD Transplant Hepatology fellowship and completed a master's degree in clinical research and studies on acute

liver failure (ALF) and organ donation with Dr. Fontana while at U-M. He is now Associate Professor of Medicine at the University of Kansas liver transplant program and continuing to conduct studies on ALF and viral hepatitis.

**DR. AMIT SINGAL** (2010) completed several database projects as well as studies of serum biomarkers of liver cancer during his fellowship at U-M. After joining the faculty at University of Texas Southwestern Medical Center, he has accrued extensive

grant funding and research awards to further study the epidemiology and causes of liver cancer.

After obtaining her master's degree in clinical research, **DR. MINA RAKOSKI** (2012) pursued studies in palliative care during her transplant hepatology fellowship and assumed a faculty role after graduation.

As a transplant fellow, **DR. JESSICA MELLINGER** (2014) completed studies in alcoholic liver disease and access to care. Since joining the faculty in 2014, Dr. Mellinger was awarded the highly competitive Sheila Sherlock award from the AASLD as she prepares for her K-award funding.

**DRS. MOHAMMED JAFRI** (2010), **RINA SALGIA** (2014), **JOHN BASSETT** (2010) and **SHANNON TUJIOS** (2010) have gone on to become teachers and leaders in other major liver centers around the country, disseminating the expertise they gained at U-M.

That expertise comes from rigorous training. Fellows hold their own weekly hepatology and transplant clinics where, with direct supervision from faculty, they learn how to diagnose and treat patients with acute and chronic liver disease. In addition to rotations through the inpatient service, pathology and pediatrics, fellows also complete at least one academic research project that they publish or present at a scientific meeting.

Behind the fellows' success is a team of dedicated hepatologists who are recognized nationally for their contributions to research, training and clinical care of patients with advanced liver disease.

"What drives our program is the caliber of our fellows and of our faculty, whose goal is to offer the best possible training on a consistent basis," said Dr. Fontana. "The fruits of those efforts are graduates who establish their own successful careers, contribute to research and improve outcomes for patients with liver disease both here and around the country."



Robert J. Fontana, MD



Jessica Mellinger, MD, MSc



## Developing Expertise in Advanced Endoscopy

Advanced endoscopic procedures, including endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP), are critical to the diagnosis and treatment of many gastrointestinal disorders, and they require a high level of clinician skill. To prepare trainees, the Division offers a fourth year, 12-month Advanced Endoscopy Fellowship to physicians who have completed a three-year Gastroenterology fellowship.

"It's an unusual training program in that our faculty provide fellows with a broad perspective and any number of opportunities, both from the procedural and intellectual standpoints," said **JAMES SCHEIMAN, MD**, director of the program. Dr. Scheiman is also involved nationally in efforts to assess ERCP quality and how both trainees and experienced practitioners alike can improve skills and outcomes.

The University of Michigan Advanced Endoscopy Fellowship program's

eight faculty have extensive experience with EUS and ERCP. The program performs approximately 1,500 procedures annually, giving trainees significant clinical opportunities. Trainees also gain exposure to state-of-the-art stenting and mucosal resection and ablation techniques as well as balloon-assisted enteroscopy.

Another distinguishing feature of the program is its scholarly focus. Fellows run a dedicated, bi-weekly case conference in collaboration with active faculty and hepatobiliary

surgeons, attend a broad array of conferences and are expected to make their own research contributions.

"Here at U-M," Dr. Scheiman said, "we not only train our fellows to perform these complex procedures; we continually and critically assess the literature and apply it to improving the care of our patients."

The Division has had a formal fellowship since 2008, 17 trainees, 12 in academic practice. Prior to formal fellowship senior members of the group have mentored many

leaders in endoscopy research and practice, including Drs. Michael Kochman, Uri Ladabaum and Joe Elmnuzer, and a long list of others.

Our Fourth-year fellows have contributed research on the role of endoscopy in pancreatic cyst management as well as chronic pancreatitis and endoscopic techniques for complex polypectomy.



**JAMES M. SCHEIMAN, MD**

**ENDOSCOPIC ULTRASOUND PROGRAM**

The endoscopic Ultrasound (EUS) program, started in 1993, has grown from the first providers of this major endoscopic innovation in the State of Michigan to an internationally recognized program of excellence in clinical care, teaching and research. EUS revolutionized the care of patients with known or suspected GI malignancy, particularly of the pancreas, dramatically changing the diagnostic landscape for patients with pancreatic neuroendocrine tumors as well as adenocarcinoma. The program pioneered the use of EUS in minimally invasive therapeutic applications. The majority of advanced endoscopists in the region as well as many leaders in endoscopic research and clinical care trace their roots to the University of Michigan EUS training program.

Illustration: Bill Burgard



Jami Kinnucan, MD

### **IBD Training:**

#### PREPARING TRAINEES FOR THE COMPLEX DEMANDS OF TERTIARY IBD CARE

As recent discoveries have advanced the understanding and treatment of inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, "the management of IBD has become much more complex," said **JAMI KINNUCAN, MD**, a specialist focusing on IBD education. "This increasing complexity demands additional training for our fellows."

Dr. Kinnucan has created a new IBD training curriculum for the Division's categorical fellows that focuses on the multidisciplinary management of IBD patients. Fellows rotate on the inpatient service, manage postoperative IBD patients and participate in outpatient continuity clinics. They are actively involved in multidisciplinary conferences, a monthly IBD journal club and weekly IBD radiology teaching rounds.

In addition, Dr. Kinnucan and two current categorical fellows, **DR. PAUL CORSELLO** and **DR. ANAND PATEL**, are piloting an IBD Core Training Curriculum for fellows with clinical

and research interests in IBD. The curriculum focuses on outpatient management, endoscopic assessment and management and postoperative care of IBD patients as well as scholarly contributions.

"Tertiary care of patients with IBD requires a trainee to focus their clinical training to maximize exposure to this complex disease state," said Kinnucan. "Our curriculum not only incorporates current literature but also addresses many of the gaps in IBD training that fellows nationally have identified."

Many trainees in the program have gone on to become faculty at

U-M, under the direction of **PETER HIGGINS, MD, PhD, MSc**, and other senior IBD faculty. And other graduates have joined academic medical centers throughout the country.

"What makes our program unique is that our categorical Gastroenterology fellows are able to personalize their training to acquire the knowledge and experience they will need in practice to care for their patients with IBD," said Dr. Kinnucan. "For me, the ability to watch trainee physicians build their knowledge to manage complex patients on their own is incredibly rewarding."



Peter Higgins, MD, PhD, MSc

## Roadmap to Leadership:

NEW PROGRAM TO TRAIN FELLOWS IN BUSINESS AND POLICY ASPECTS OF GI

Throughout its 75-year history, faculty in the University of Michigan Division of Gastroenterology and Hepatology have provided strong leadership—guiding professional societies, serving as editors of major journals, helping to shape healthcare policy.



John Allen, MD, MBA

Trainees in fellowship programs around the country may be inspired by these GI leaders, but many aren't sure how they themselves might advance to serve in similar ways.

"Currently, no real roadmap exists to help young physicians—in community practice or academia—learn how to progress up the ladder to lead organizations, including medical practices," said **JOHN ALLEN, MD, MBA**, professor of medicine.

Dr. Allen himself has held many leadership roles in the past; he was president of the American Gastroenterological Association and also served as clinical chief of digestive diseases at Yale University. He helped establish a large, single-specialty GI practice in Minnesota with more than 60 physicians, and developed its nationally recognized quality program.

Now on the U-M GI faculty, Dr. Allen is working on a novel program to help fellowship trainees gain the knowledge and experience to chart their course toward professional leadership.

"In talking with fellows all over the country, one of the things they've identified as missing from their training is information about how to run the business aspects of their lives and careers—be it job searches, starting a community-based ambulatory surgery center or running a successful laboratory or clinical research program in academia," he said. "They know they need to make informed decisions about where they want to take their

careers, but they aren't sure how to break into those circles."

The new program, tentatively named "Life, Leadership and Legacy" and scheduled to begin in mid-2017, will educate interested fellows in career planning, financial and practice management, organizational leadership and healthcare policy.

The program will draw upon the University's wealth of resources and expertise in many disciplines as well as from external professionals, including policymakers and leaders of large GI practices.

Such broad and deep expertise will enable a flexible, highly individualized approach, giving fellows options to pursue further training in specific areas of interest.

The GI division's program will be one of the only, if not *the* only, GI fellowship program to make business and professional leadership an integral part of traditional fellowship training.

"Not many places have the capabilities that U-M does to create a program such as this," said Dr. Allen, who will leverage those capabilities for an important purpose: "We plan to make the University of Michigan the place for training future GI leaders."



## **Basic, Clinical + Translational Research**

Basic and translational research is a major mission of the Division. Physician scientists, clinical investigators and master clinicians work together seamlessly to ensure that many basic science observations are translated into clinical applications.

For example, the discovery of a trypsin-sensitive CCK releasing factor, which stimulates CCK release, provided the basis for understanding the clinical utility of pancreatic enzyme supplement in alleviating pain in chronic pancreatitis. The observation that somatostatin has both excitatory and inhibitory actions in myenteric cholinergic transmission and thus, plays a critical role in mediating both limbs of the peristaltic reflex, led to the use of Octreotide in the treatment of chronic intestinal pseudoobstruction.

## Embracing Practice Through Discovery

The GI Peptide Center (P30 DK034933) is the epicenter of the Division's research enterprise. Funded since 1984, the Center today has 58 primary investigators and four major Service Cores to support GI research related to signal transduction mechanisms governing homeostasis and GI disorders. The approach includes studies on genetics and gene regulation, cellular signaling pathways, receptors and ion channels. Research themes include: 1) Neurobiology of visceral pain, enteric motility and appetite control; 2) Molecular and cellular mechanisms of gut inflammation; and 3) Cell growth, differentiation and programmed cell death. The Center currently has a research base of \$26.8 million in digestive disease-related funding representing nearly 10 percent of the total research base of the University of Michigan Medical School.

In addition to multiple National Institutes of Health (NIH) R01, U01, and K08/K23 grants, the Division currently has two major Program Projects through NIH P01/U54 mechanisms. In 2002, **DR. JUANITA MERCHANT** in collaboration with **DR. DEB GUMUCIO** (Department of Cell and Developmental Biology), **DR. LINDA SAMUELSON** (Department of Molecular and Integrative Physiology) and **DR. ANDREA TODISCO** (Division of Gastroenterology and Hepatology) successfully initiated a Program Project P01 DK062041 to investigate cellular decisions in the GI tract. The underlying theme focuses on the interplay between developmental signaling pathways and environmental cues to direct cell specifications, homeostasis and metaplasia, a pre-neoplastic change. This grant has

been funded for 10 years and was renewed in 2013 for another five years.

The second Program Project was initiated by **DR. THOMAS WANG** in 2011. This GI Molecular Imaging Program was funded by the National Cancer Institute (NCI) through U54 mechanisms (U54 CA163059). Using peptides as a novel probe platform, Dr. Wang has developed imaging agents with high specificity and binding affinity to over-express or gene-amplified targets on the surface of cancer and precancerous cell types. During endoscopy these peptide probes can be fluorescently labeled and applied in high concentration to the mucosa for detection by dual-axis confocal microendoscopy.

In this way, Dr. Wang and colleagues can perform real time "optical biopsies"

for the early detection of precancerous or cancerous lesions. Currently the technique shows promising applications for early detection of Barrett's Esophagus and early colonic neoplastic changes in patients with inflammatory bowel disease. His team includes **DRS. JOEL RUBENSTEIN, ELENA STOFFEL** and **KIM TURGEON** and is supported by a group of dedicated study coordinators led by **ELAINE BRADY**. The total NCI funding amounts to \$11.8 million over five years.

The Division takes pride in the fact that 44 percent of its 75 faculty are Physician Scientists. Most of the research is funded through NIH/NCI or the U.S. Department of Veterans Affairs (VA) system. Currently the Division has 15 R01/R37 grants, 7 U01/U54, 3 P01/P30, and 6 K08/K23 grants, and

our physicians based at the VA have received multiple VA Merit and Career Development Awards.

Clinical Investigation is a major focus of our research enterprise. In 2016 the Division had 13 foundation grants, 12 investigator-initiated pharmaceutical studies, and 84 clinical trials. The combined total of all grants in the Division is 167, totaling \$16 million of annual funding, making our Division one of the most highly funded GI divisions in the country.

Our rich tradition of basic and clinical research enhances our clinical practice with innovative approaches and new treatments for patient care. Our physicians embrace practice through discovery.

## Discovery and Scientific Achievement:

### MICHIGAN GASTROINTESTINAL PEPTIDE RESEARCH CENTER

**TACHI YAMADA, MD**, and **CHUNG OWYANG, MD**, established the Michigan Gastrointestinal Peptide Research Center (MGPRC) and National Institutes of Health/National Institute of Digestive and Diabetes and Kidney Diseases-funded Silvio O. Conte Digestive Diseases Research Center in 1984. MGPRC is the only center in the nation devoted to the study of GI peptides in the pathophysiology, diagnosis and treatment of GI disorders. Work in the Center has yielded a number of seminal findings over the years, which have been translated into new treatment approaches and improved outcomes for patients.

"Since its founding, the MGPRC has been the engine that drives our research initiative," said Dr. Owyang, H. Marvin Pollard Professor and Division chief since 1990. "It's the heart and soul of our translational research enterprise in many ways."

Dr. Yamada, who served as Division chief from 1983 to 1990, was the first to apply molecular biology techniques to the study of biochemistry and physiology of gut hormones. A major breakthrough was his isolation and characterization

of glycine extended processing intermediates of gastrin. This seminal work provided the tools for examination of substrate specificity of the carboxyl terminal amidation reaction, which is of critical importance in the biological activation of nearly 50 percent of all peptide hormones known today (*Science*, 1994; 265: 440-442).

Dr. Yamada went on to characterize specific receptors for glycine extended gastrin, providing the first insight into the possibility that

peptide hormone precursors may have unique functions separate and distinct from their end products.

With support of the MGPRC, Dr. Owyang's lab discovered that somatostatin both excites and inhibits myenteric cholinergic transmission and plays a crucial role in mediating both limbs of the peristaltic reflex. This led to the use of somatostatin to treat small bowel bacterial overgrowth in patients with chronic intestinal pseudo obstruction (*New England Journal of Medicine*,

1991; 325: 1461-71). It was the first instance where a peptide was used to treat a GI disorder.

Dr. Owyang's laboratory also characterized a new peptide, CCK-releasing peptide, which is secreted into the intestinal lumen in response to food and stimulates CCK release. Pancreatic enzymes subsequently secreted into the lumen inactivate CCK-releasing peptide, thereby creating a feedback regulating loop (*Proceedings of the National Academy of Sciences*, 1996; 93: 7927-32). This novel observation provided the basis for understanding the clinical utility of pancreatic enzyme supplements in alleviating pain in chronic pancreatitis patients by diminishing CCK-mediated stimulation.



Tachi Yamada, MD, KBE



Richard C. Boland, MD

In 1995, **RICHARD C. BOLAND, MD**, uncovered the role of DNA mismatch repair in regulating the G2/s cell cycle checkpoint and predicted that colon cancer with microsatellite instability would be resistant to chemotherapy (*Cancer Research*, 1995; Sep 1;55(17):3721-5).

This set the foundation for subsequent studies on colon cancer genetics.

More recently, using a large, prospectively identified cohort of patients with acute liver failure, **BISHR OMARY, MD, PhD**, identified keratin 8/18 as important susceptibility genes for acute liver failure development. His studies demonstrated that ethnicity-selective keratin variants predisposed carriers to death or the need for liver transplantation when these subjects develop acute liver failure, raising the possibility of using K8/K18 variants as prognostic biomarkers. Collectively, these findings provided a unique link of the cytoskeleton to liver failure (*Gastroenterology*, 2010; 139: 828-835).



Nobu Kamada, PhD

The groundbreaking work of **NOBU KAMADA, PhD**, and **GABRIEL NUNEZ, MD**, has shown that a host's immune system and commensal bacteria work together to control enteric pathogen infections. Their research finds that mouse-pathogenic *E. coli* *Citrobacter rodentium* employs its virulence



Chung Owyang, MD



Bishr Omary, MD, PhD



Gabriel Nunez, MD

factors to find a location within the epithelial niche in order to evade commensal bacteria. In response, the host develops specialized IgG to neutralize these virulence factors. This process forces the pathogens to relocate from the epithelial niche to the intestinal lumen, where they are outcompeted by commensal

microbes for nutrients (*Science*, 2012; 336(6086):1325-9; *Cell Host Microbe*, 2015; 17(5):617-27).

**JUANITA MERCHANT, MD, PhD**, clarifies the mechanisms by which *Helicobacter pylori* infection causes gastric metaplasia and cancer, by showing that dying parietal cells release Sonic Hedgehog, recruiting inflammatory cells that over time become immunosuppressive. The Hedgehog-dependent immune cells create a pre-neoplastic microenvironment in the stomach. Molecular signatures from these myeloid-derived suppressor cells (Schlafens) are being tested as potential biomarkers in patients infected with *Helicobacter pylori*.

A second major project in the Merchant laboratory has identified a novel mechanism for Men1-dependent neuroendocrine tumors. Dr. Merchant's lab is the first to develop a mouse model of gastric carcinoid tumors (*Gut*, 2016; 0:1-10. doi:10.1136/gutjnl-2015-310928).

**ELIZABETH SPELIOTES, MD, PhD**, utilized human population-based and functional genetic studies and showed that genetic etiology of obesity and nonalcoholic fatty liver disease (NAFLD) are influenced by genes in the nervous system, in adipose tissue and in the liver. Her laboratory found that genes play a role in neuronal processes, energy expenditure, eating behavior and predispose to development of overall obesity, whereas pathways that



Elizabeth Speliotes, MD, PhD, MPH

affect lipid and glucose metabolism predispose to development of NAFLD. Dr. Speliotes' studies provide new insights into the pathophysiology of these disorders and identify new targets for therapy. (*Nature*, 2015; Feb 12;518(7538):197-206; *PLoS Genetics*, 2011; Mar;7(3):e1001324).

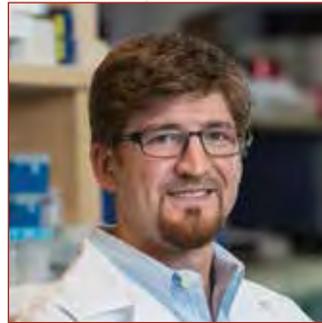


Thomas Wang, MD, PhD

**THOMAS WANG, MD, PhD**, earned his PhD in biomedical engineering, pioneered the use of fluorescence-labeled peptides for the early detection of cancer in the GI tract. He developed peptide probes by screening for high-affinity ligands that bind preferentially

to premalignant lesions such as Barrett's Esophagus (*Science Translational Medicine*, 2013; 5:184rab1) and colorectal cancer (*Nature Medicine*, 2008; 14:454-58). This novel methodology uses endoscopy to target disease in the premalignant stage to reduce the incidence, morbidity and mortality of esophageal and other cancers.

**JASON SPENCE, PhD**, and his lab are on the forefront of generating 3D models from pluripotent stem cells. He described a human intestinal organoid model during his postdoctoral studies, is involved in efforts to generate additional 3D models (*Stem Cell Reports*, 2015; Jun 3. pii: S2213-6711(15)00122-8) and has implemented these models to study developmental



Jason Spence, PhD

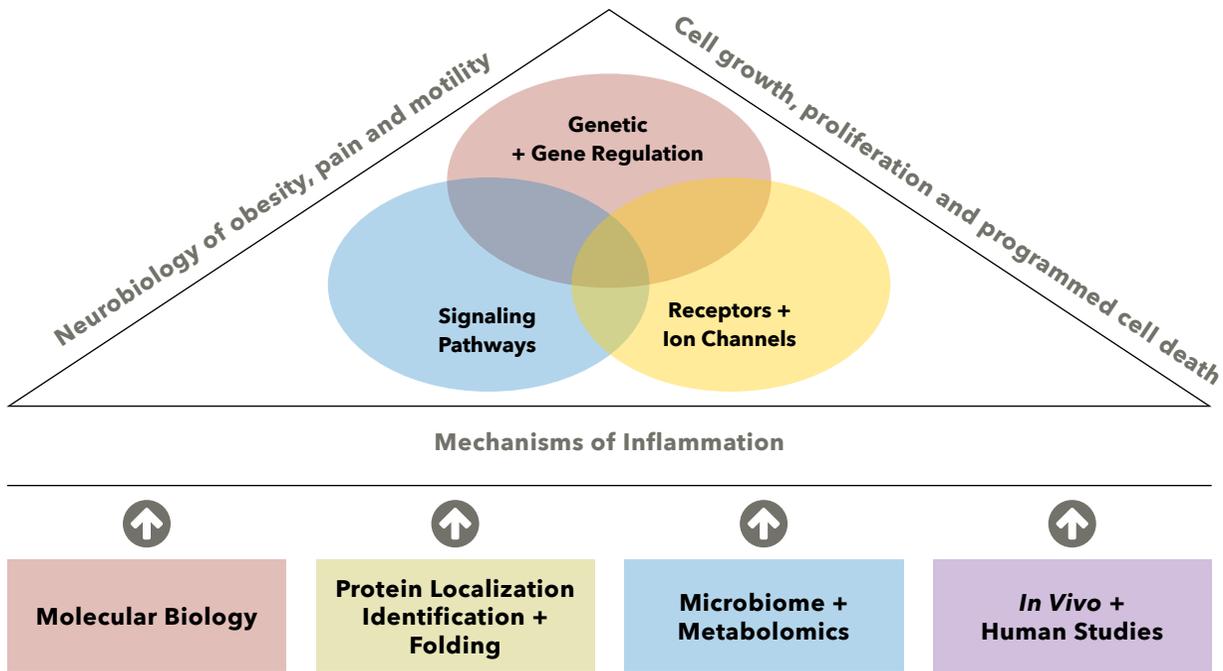
biology of epithelium and disease (*eLife*, 2016; Sep 28;5. pii: e19732. doi: 10.7554/eLife.19732). One year after Dr. Spence arrived at U-M, the GI Division committed \$100,000 to develop the Organoid/Enteroid Modeling Program for the Center. This paradigm shifting set of

technologies offers a new toolkit for scientists to study human epithelial development, homeostasis and disease *in vitro*.

Over the Center's three-decade history, research has shown that many gut peptides in fact extend beyond their classical role as hormones to also act as paracrine effectors, neurotransmitters, growth factors and cytokines. Hence, in 2014, we changed the name of the Center to the University of Michigan Center for Gastrointestinal Research (UMCGR) to more accurately reflect its comprehensive mission.



Juanita Merchant, MD, PhD



In its current configuration, the overarching goal of the Center is to investigate signal transduction mechanisms regulating homeostasis and GI disorders. Our approach includes studies on genetics and gene regulation, cellular signaling pathways, receptors and ion channels. The approach will be utilized by the three major research themes reflecting the common research interests of numerous investigators affiliated with the Center. Our research themes include 1) Neurobiology of visceral pain, enteric motility and appetite control, 2) Molecular and cellular mechanisms of gut inflammation and 3) Cell growth, Differentiation and Programmed Cell Death.

**Impact**

Today, the Center includes 58 primary investigators, four major research service cores and a number of educational programs including symposia and the Yamada Lectureship. The Center also encourages and supports new areas of related research and talent development through pilot project funding.

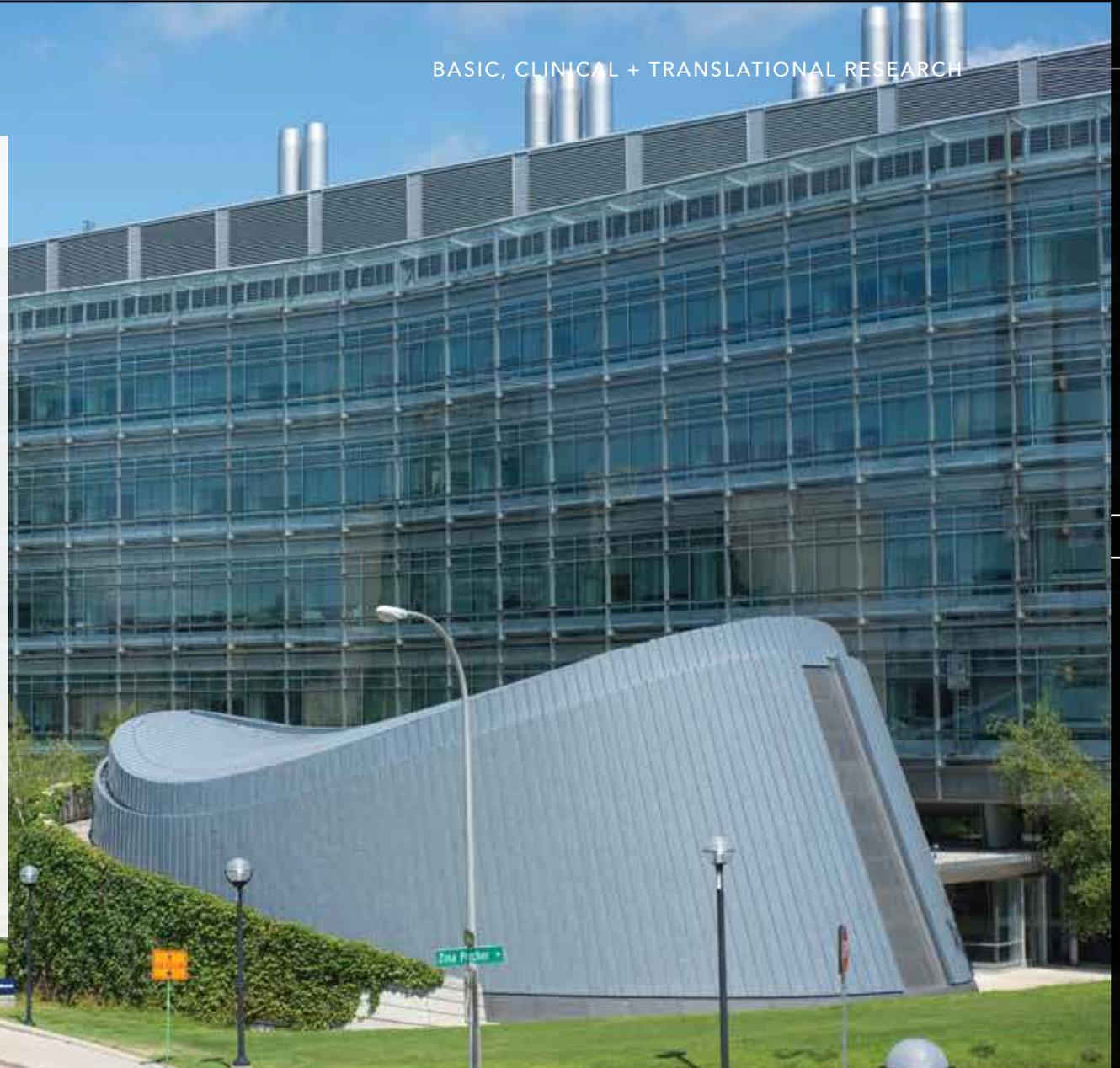
The impact of the Center's focus cannot be overstated. Funding for research related to this Digestive Disease Center, currently \$26.8 million in digestive disease-related funding (48 percent from NIDDK) and \$16.6 million in other research grant support, represents nearly 10 percent of the total research base of

the University of Michigan Medical School. In addition, significant institutional support (\$1 million) has been amassed to support Center objectives. It has broadened the research scope of individual laboratories and greatly expanded interest in digestive disease-related research. Center investigators have been extremely productive during the last five-year funding period, contributing 519 publications as a result of the core services provided through the UMCGR.

Additionally, as a testament to the Center's Pilot and Feasibility program's success, for the past 10 years projects representing a total investment of \$1,050,000 in direct costs, (\$1,577,500 total costs) have generated 20 NIH awards (2 K08, 2

R21, R03, R00, 2 U01, U19 and 11 R01s) totaling \$18,132,140 in direct costs (\$27,142,287 total costs); a 17-fold return on investment.

Continuously funded for over 30 years, The University of Michigan Center for Gastrointestinal Research, in short, has become the fulcrum of activity that galvanizes the efforts of the large and established group of investigators involved in gastrointestinal research that exists at the University of Michigan.



## Host Microbiome Initiative:

### UNDERSTANDING THE ROLE OF GUT MICROBIOTA IN HEALTH AND DISEASE

In 2013, the University of Michigan Medical Center developed the Host Microbiome Initiative (HMI) under the co-directorship of **DRS. VINCENT YOUNG** and **HARRY MOBLEY**. This initiative has played a significant role in supporting GI faculty who are investigating host microbiome interactions in health and GI disorders to further promote research on the role of microbiome in IBD, IBS and metabolic disorders. The Center for Gastrointestinal Research developed a Microbiome and Metabolics CORE. With this support, a number of divisional faculty are making important discoveries in the diagnosis, treatment and management of a number of gastrointestinal disorders.

"The Host Microbiome Initiative is an incredible resource for the Division's



John Kao, MD

scientific and clinical investigators—and for other investigators across campus," said **JOHN KAO, MD**, associate professor and gut microbiome investigator in the HMI. "The HMI has the expertise to perform comprehensive analysis of microbial communities, which enables us to study the function of gut microbiota in health and disease."

The HMI serves as a hub of microbiome-related research for Division faculty. Dr. Kao and colleagues

in Infectious Disease have established a clinical protocol using fecal microbiota transplantation in treating patients with recurrent *Clostridium difficile* (*C. diff*) infection (*American Journal of Gastroenterology*, 2014; 109:1065-1071). The U-M was one of the first institutions in the country to perform these transplants under FDA protocol.

Extending the work, **VINCE YOUNG, MD, PhD**, co-director of the HMI, has published findings related to recovery of the gut microbiome following trans-

plantation (*mBio*, 2014; 5(3):e00893-14). Dr. Young also used untargeted metabolomics analysis in a mouse model of *C. diff* infection to show that antibiotic-induced loss of colonization resistance against *C. diff* was associated with relative increases in primary bile acids and a corresponding decrease in secondary bile acids, an environment that favors *C. diff* germination and increases disease susceptibility after antibiotic treatment (*Nature Communications*, 2014; 5:3114).

The dynamic interaction of a pathogen with the resident gut microbiota was investigated by **NOBU KAMADA, PhD**, a research faculty member in the Division. Dr. Kamada proposes that competition between resident microbes and pathogens is influenced by the expression of virulence factors by pathogens and by the

Gram stain of mouse ileum showing the interface between intestinal epithelium and gut microbiota.

Photo: Kathryn Eaton



Vince Young, MD, PhD

nutritional requirements of both populations (*Science*, 2012; Jun 8;336(6086):1325-9).

Dr. Kao and **CHUNG OWYANG, MD**, are investigating how the antibiotic rifaximin, recently approved for patients with irritable bowel syndrome (IBS) with diarrhea, affects the microbiome following treatment in rat models, including the expan-

sion of beneficial probiotic species (*Gastroenterology*, 2014; 146(2): 484-496). In another study, Dr. Kao is identifying biomarkers that signal dysbiosis (*Gastroenterology*, 2015; 149 (7): 1849-1859).

The two also are investigating the role of the microbiome in models of stress-induced hypersensitivity—akin to IBS in humans—in mice (*Gastroenterology*, 2013; 144(7): 1478-1487). The researchers found that stress changes the composition of gut bacteria and that the microbiome indeed plays a functional role in causing symptoms, including inflammation in the colon, in stressed animals.

In a collaborative research effort between U-M and Peking University through the Joint Institute for Translational and Clinical Research, Drs. Owyang and Kao are leading an

ongoing project to identify differences in gut microbiota in healthy subjects and in IBS patients following either a meat- or plant-based diet. Studies will be conducted in Beijing and Ann Arbor to understand the impacts of diet and racial factors on the gut microbiota of IBS patients.

Additional research into the relationship between the microbiome and IBS include studies by **WILLIAM D. CHEY, MD**, and **SHANTI ESWARAN, MD**, to characterize patient microbiota and the impact of a low-FODMAP diet.

**ELENA STOFFEL, MD, MPH**, is examining the microbiome in families with familial polyposis to try to identify communities associated with more vs. less severe polyposis.

**HARI CONJEEVARAM, MD, MSc**, is looking at the role of the microbiome in non-alcoholic fatty liver disease

(NAFLD)/non-alcoholic steatohepatitis (NASH), a condition increasing in prevalence globally. He is also looking into the role of fecal microbiome transplantation (FMT) in the management of NASH. Part of this work is currently in collaboration with investigators at the All India Institute of Medical Sciences (AIIMS) in New Delhi, India, where there has been a rise in prevalence of NAFLD, and the pathophysiology, including the role of diet, might differ from that seen in Americans.

In patients with ulcerative colitis (UC), **PETER HIGGINS, MD, PhD, MSc**, is looking at the microbiome at the time of UC flares, during *C. diff* infection and after recovery from *C. diff* infection to learn whether recovery of microbial diversity might predict whether patients will develop a recurrence of *C. diff* infection or UC flare and to identify which species are present or absent in

patients who develop recurrences. The findings and subsequent work may inform new probiotic-based therapies to lessen the risk of complications from recurring flares and infection.

“The HMI is critical to the Division’s research,” said Dr. Kao. “Not only does the HMI make us more competitive in securing funding because of the unparalleled expertise it provides us as investigators; it also supports important work that leads us to new ways of improving the health of our patients.”

## Organogenesis:

GENERATING NEW HUMAN MODELS OF ORGAN DEVELOPMENT AND DISEASE



Jason Spence, PhD

Gastrointestinal organoids, or complex, three-dimensional GI tissues derived from human and induced pluripotent stem cells, are providing new and invaluable insights into human organ development and disease pathogenesis. Such insights may one day lead to more personalized approaches to medical treatment.

“Organoids represent a unique tool in our experimental toolbox,” said **JASON SPENCE, PhD**, associate professor in the departments of Internal Medicine, Gastroenterology and Cell and Developmental Biology. “They can yield a tremendous amount of information when used as models to study human disease *in vitro*, and they are a platform that enables new translational research.”

Unlike many traditional cell lines that have been derived from cancer, organoids represent a renewable source of healthy tissue. And while typical cell culture lines are relatively homoge-

neous and often represent only one type of cell, organoids represent some of the complexity of the organ from which they were derived. Human intestinal organoids (HIOs), for example, possess multiple cell types, including stem cells and differentiated cell types—Paneth, goblet, enteroendocrine cells and enterocytes.

The Spence Laboratory uses organoids grown from the stem cells of patient tissue (*Stem Cell Reports*, 2015; Jun 3: (15) 00122-8) taken during biopsy, which provides opportunities to study both healthy and diseased tissues from adult humans.

In addition, Spence also demonstrated a process to direct the differentiation of human pluripotent stem cells into intestinal tissue *in vitro* (*Nature*, 2011; 470: 105-109). The resulting HIOs contained all major cell types, as well as a mesenchymal layer that simultaneously developed with the epithelium.

Building on that work, the Spence Laboratory has recently shown that pluripotent stem cell-derived HIOs are similar to the immature, fetal small intestine, specifically the duodenum, and that when transplanted into mice they mature into adult-like tissue (*Stem Cell Reports*, 2015).

The laboratory has focused recent efforts on understanding how different regions of the intestine gain their identity during embryonic development and how the intestine becomes mature and fully functional. “This type of information is critical to using these systems in the appropriate way—we have to match the correct organoid system to the correct scientific question,” Spence noted.

Given their uses for discovery and translational research, organoids help investigators move beyond modeling health and disease in animals to studying human health and disease in human tissue. “Models such as organoids bring together basic scientists asking fundamental biological questions with clinical scientists who are interested in understanding disease,” said

Spence, who co-authored the textbook *Translational Research and Discovery in Gastroenterology: Organogenesis to Disease* (Wiley, 2014).

Some of those questions relate to *Clostridium difficile* (*C. diff.*), an epidemic infection in U.S. hospitals. It infects the colon and can cause death in up to 7 percent of elderly patients. New therapies, including blocking antibodies and new antibiotics are being developed to fight this infection. *C. diff.* bacteria can be microinjected into human gut organoids to reproduce the infection in the lab. In organoids, the infection breaks down the ability of the gut lining to maintain barrier function and allows invasion between epithelial cells. With the use of organoids, laboratory experiments to understand how infections such as *C. diff.* invade the

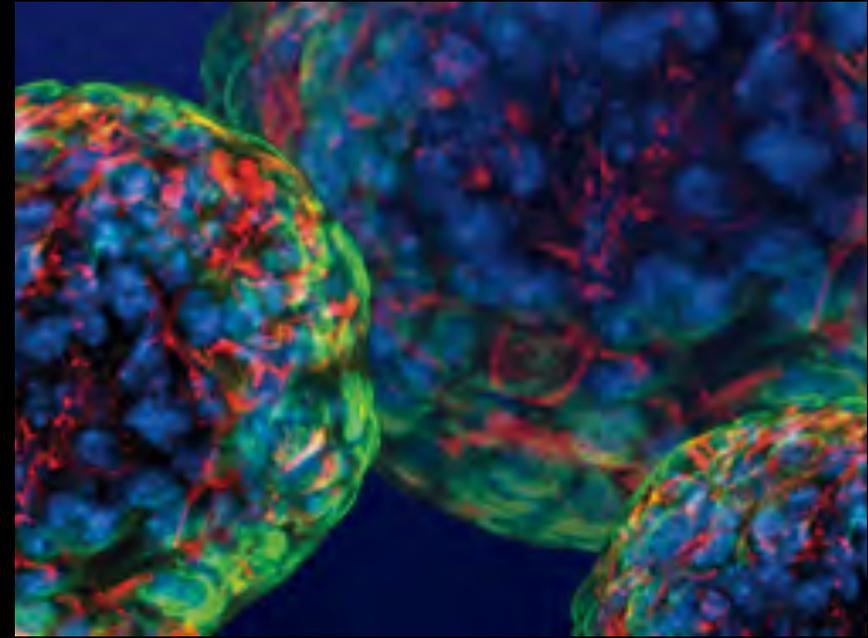
gut, and how to treat these infections, can be conducted rapidly, thereby quickly advancing new treatments.

In **DR. PETER HIGGINS'** lab, his team studies the scarring and fibrosis in inflammatory bowel disease that causes bowel damage and requires surgery in three quarters of patients with Crohn's disease. Dr. Higgins' group has been able to identify the pathways that cause intestinal fibrosis in organoids and can mimic the fibrotic process that occurs in human intestines. With this gut organoid fibrosis system, they can test new anti-fibrotic medications on human gut organoids. Early successes with this approach are encouraging as a method to develop and test new therapies for gastrointestinal diseases and rapidly determine if they work in human tissues.

"Basic and clinical scientists both want to apply the same tool to answer different questions, and the scientific overlap creates natural synergies," Spence said. "The strong commitment to both clinical and basic sciences, and the breadth and depth of expertise at the University of Michigan, make it an ideal place to conduct this kind of translational research."



Peter Higgins, MD, PhD, MSc



Human intestinal organoids used to identify targets for anti-fibrotic drug development

## Physician-Scientists:

ADVANCING BASIC SCIENCE RESEARCH AND DISCOVERY

The University of Michigan Gastroenterology Fellowship Program helps trainees develop both the clinical and research skills that prepare them for careers in academic medicine. Fellows choose from one of two tracks, Clinical or Basic Science, both of which fulfill ACGME requirements.

Fellows selecting the Basic Science Track will be supported by a National Institutes of Health (NIH) T32 grant dedicated to training fellows in basic and translational digestive sciences (T32 DK094775). They will spend time in Division laboratories, conducting basic science and translational research. Many of the Division's Basic Science fellows are part of the Physician Scientist Training Program (MD-PhD), in which they undertake accelerated training in Internal Medicine for two years, followed by ACGME-required training in clinical gastroenterology for a minimum of 18 months. The remainder of fellows'

six-year training is dedicated to National Institutes of Health-funded research. Currently, about 40 percent of the Division's faculty are physician-scientists. Some examples of our trainees and their work include:

*Understanding the role of visceral sensation in functional GI disorders*

**JOHN W. WILEY, MD**  
(Fellowship 1984)  
Professor, Internal Medicine  
University of Michigan

Dr. Wiley's research focuses on pain pathways that innervate the gut and how these pathways are altered in diabetes mellitus and irritable bowel

syndrome. His laboratory has identified specific changes in the regulation of ion channels located on the sensory nerves that transmit pain signals from the colon in diabetic rodent models, in aged animals and models of chronic stress. His recent research focuses on the role of epigenetic regulatory pathways in chronic stress-associated enhanced abdominal pain. Dr. Wiley's research has been continuously funded by the NIH for more than 25 years.

*"The clinical and basic research training I received at the University of Michigan positioned me*

*for a productive career in academic medicine. The mentoring and individual attention that I received played a pivotal role in my career development as an investigator, educator and research administrator."*



John W. Wiley, MD

*Investigating the Mechanisms Regulating Epithelial Cell Growth and Differentiation in the GI Tract*

**ANDREA TODISCO, MD**  
(Fellowship 1991)  
Professor, Internal Medicine  
University of Michigan

Dr. Todisco has a longstanding interest in the elucidation of the mechanisms that regulate epithelial cell growth and differentiation in the luminal gastrointestinal tract. In particular, his investigations have been focused on the intracellular signal transduction pathways that mediate the multiple, complex actions of growth factors and morphogens such as gastrin, epidermal growth factor (EGF), Sonic Hedgehog (Shh) and the bone morphogenetic proteins (BMPs) in the stomach. His most recent investigations, centered

on the role of BMP signaling in gastric inflammation and carcinogenesis, have involved the use of both primary cultures of gastric epithelial cells and transgenic mice. These studies have unraveled novel and important mechanisms that appear to play a significant role in the pathophysiology of gastric dysplasia and neoplasia.

“My fellowship at the University of Michigan has been instrumental to the establishment of my academic career. I had the fortune to work with an exceptional mentor and with outstanding colleagues in an intellectually

stimulating and nourishing environment. Without the support and the teaching that I received as a GI fellow, I could never be able to pursue my academic and investigative goals.”



Andrea Todisco, MD

*Investigating metabolic interactions between gut microbiota and host*  
**GARY D. WU, MD** (Fellowship 1992)  
 Professor of Medicine  
 Ferdinand G. Weisbrod Chair in Gastroenterology  
 Co-Director PennCHOP Microbiome Program  
 University of Pennsylvania

Current research programs in the Wu laboratory focus on the mutualistic interactions between gut microbiota and the host with a particular focus on metabolism. Current areas of investigation include the effect of diet on the composition of the gut microbiota and its subsequent effect on host metabolism related to nitrogen balance as well as its impact on metabolic pathways in the intestinal epithelium, principally fatty acid oxidation.

Dr. Wu is also directing a project investigating the impact of diet on the composition of the gut microbiome and its relationship to therapeutic responses associated with the treatment of patients with Crohn’s disease using an elemental diet.

Finally, Dr. Wu is leading a multidisciplinary group of investigators using phosphorescence nanoprobe technology to examine the dynamic oxygen interaction between the host and the gut microbiota at the intestinal mucosal interface.

“The training I received as a GI research fellow at the University of Michigan not only introduced me to the tremendous professional

rewards and opportunities in pursuing a career as a physician-scientist but also taught me the cognitive and technical skills that were essential to becoming an independent investigator.”



Gary D. Wu, MD

*Understanding the biology of colon cancer*

**JOHN CARETHERS, MD**  
(Fellowship 1995)  
John G. Searle Professor and Chair,  
Department of Internal Medicine  
University of Michigan

Dr. Carethers' current research direction is focused on colorectal cancer—in particular, defective DNA mismatch repair, which drives the most common type of hereditary colorectal cancer, Lynch syndrome, as well as more than 15 percent of sporadic, non-familial colorectal cancer. His current NIH-funded projects address the function of one of the DNA mismatch repair proteins, the role of inflammation and regulation of the DNA mismatch repair system, and some racial/ethnic differences in the occurrence of defective DNA mismatch

repair and its relationship to outcome and survival for these patients.

“The Physician Scientist track during my GI fellowship at Michigan enabled me to pursue research with a fantastic mentor, Rick Boland, who happened to make a transformative change in his research from biochemistry to genetics at the time I joined his lab. The track provided some protected research time after my clinical GI training, plus it enabled me

to focus on projects that led to my development in writing papers and grants, something I had to learn how to do. Without this track, I would not be where I am today.”



John Carethers, MD

*Understanding the enteric nervous system in health and disease*

**SHANTHI SRINIVASAN, MD**  
(Fellowship 1999)  
Professor of Medicine, Emory  
University  
Chief of Gastroenterology, Atlanta  
VAMC

Current research programs in the Srinivasan laboratory focus on the mechanisms of altered gastrointestinal motility by understanding the development and pathophysiology of the enteric nervous system. Current areas of investigation include the effect of a high fat diet on gut microbiota and its subsequent effect on altered gastrointestinal motility. Her laboratory has demonstrated the role of the pathogen recognition receptor TLR4 in regulating the development of the enteric

nervous system. By understanding the interaction of gut microbiota and the enteric nervous system, Dr. Srinivasan and her laboratory hope to develop new strategies to treat gastrointestinal motility disorders.

Dr. Srinivasan is also investigating the role of neurotrophic factor GDNF and how it regulates obesity and hepatic steatosis. Recent studies have demonstrated that GDNF can improve fatty acid oxidation in the hepatocyte and lead to a reduction in hepatic steatosis.

“My interactions with the GI faculty at the University of Michigan during my fellowship sparked my interest in pursuing a career in gastrointestinal

motility-related research. The outstanding faculty, nurturing environment and opportunities helped me to achieve my aspiration to be a physician-scientist and develop my own scientific niche. I am grateful for the wonderful mentorship at the University of Michigan that enabled me to have a successful academic career.



Shanthi Srinivasan, MD

*Unraveling the principles underlying pathologic gut inflammation*

**EZRA BURSTEIN, MD**

(Fellowship 2001)

Associate Professor

Chief, Division of Gastroenterology

Department of Internal Medicine,

Division of Digestive & Liver Diseases

Department of Molecular Biology

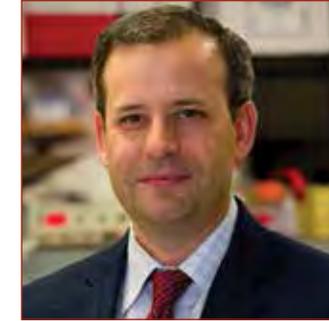
University of Texas Southwestern Medical Center

Dr. Burstein's laboratory is focused on unraveling fundamental principles behind pathologic inflammation and its role in human disease, particularly in the GI tract. A significant effort is devoted to investigation of transcriptional circuits that control the activation of pro-inflammatory genes. This work has led Dr. Burstein to discover the COMMD protein family, a group of intracellular factors that regulate pro-inflammatory signals as well as other processes, most importantly, the sorting and proper recycling of cell receptors that traverse through the endosomal compartment. In parallel to these molecular and cellular studies, Dr. Burstein's laboratory also investigates the genetic and molecular pathogenesis of disorders of altered

immune function in humans, particularly Mendelian disorders that involve abnormal gut inflammation.

*"Training at University of Michigan was an essential step in my career development. Many things had to come together for me to be able to successfully emerge from training with the prospect of developing an independent research program. After interviewing in leading programs around the country, I found that only Michigan could offer the*

*mentorship and sustained institutional support I needed and that proved key to my career development. I can say unequivocally that I owe my academic career to the vision and support that I received at U-M."*



Ezra Burstein, MD

*Probing the mechanisms of immune homeostasis regulating the gut microbiota-host interaction*

**JOHN Y. KAO, MD** (Fellowship 2002)  
Associate Professor of Medicine  
Associate Director, GI Fellowship  
Training Program

Dr. Kao's research focuses on understanding how gut microbes peacefully coexist in the GI tract with their human host and identifying factors that contribute to an altered symbiotic relationship leading to dysbiosis. His earlier NIH-funded work discovered the beneficial role of *H. pylori* colonization in lowering the risk of IBD and contributed to the current practice guideline to eradicate *H. pylori* only in symptomatic or at-risk patients. His lab continues to investigate novel immune pathways (e.g., tryptophan metabolism in B cell

development and inflammasome regulation of CD8+ T cells) of *H. pylori*-associated intestinal metaplasia.

Additional research efforts aim to understand the role of environmental (e.g., stress and diet) and host factors (e.g., Duox2 and racial differences) that contribute to altered gut microbiota with disease-causing potentials. He has translated this knowledge into clinical practice by helping to start the Fecal Microbiota Transplantation Program at University of Michigan.

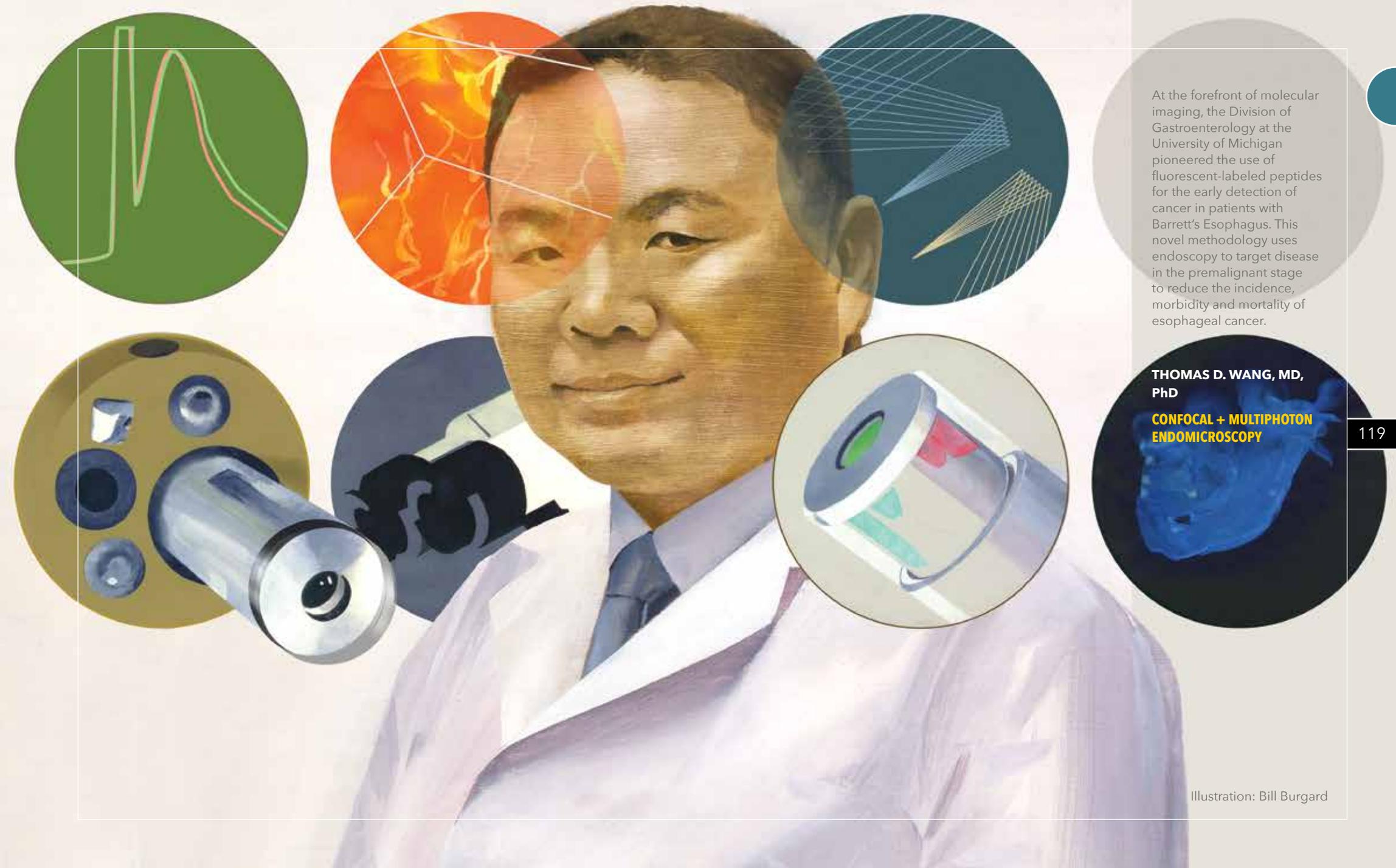
"I quickly realized after starting my GI fellowship that the Michigan Difference was the unparalleled expertise and mentorship that await those who seek a career in

academic medicine. Having no formal basic research training, I pursued the basic science research fellowship track supported by the GI division's T32 training grant and became proficient in immunological methods under the mentorship of Juanita Merchant and transitioned successfully to independence as a tenured faculty. I would have never realized my passion for scientific discovery and academic medicine if I hadn't come to Michigan, a

move seldom pursued by a Californian. Coming to Michigan was the single most important career decision my wife and I made 17 years ago. That is the Michigan Difference."



John Y. Kao, MD



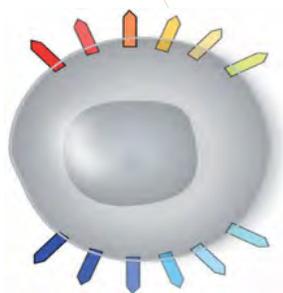
At the forefront of molecular imaging, the Division of Gastroenterology at the University of Michigan pioneered the use of fluorescent-labeled peptides for the early detection of cancer in patients with Barrett's Esophagus. This novel methodology uses endoscopy to target disease in the premalignant stage to reduce the incidence, morbidity and mortality of esophageal cancer.

**THOMAS D. WANG, MD,  
PhD**

**CONFOCAL + MULTIPHOTON  
ENDOMICROSCOPY**

## Peptide Probes and Novel Imaging Platforms to Detect Early GI Cancers

With a combination of innovations, **THOMAS WANG, MD, PHD**, the H. Marvin Pollard Collegiate Professor of Endoscopy Research, is leading a critical charge: to remove uncertainty from the diagnosis of cancer in its earliest and most treatable stages.



This goal underlies Dr. Wang's work developing new peptide imaging agents and advanced optical imaging methods in order to investigate the molecular properties of the mucosa in the digestive tract.

Using peptides as a novel probe platform, Dr. Wang has developed imaging agents with high specificity and binding affinity to overexpressed or gene-amplified targets on the surfaces of cancer and precancerous cell types. During endoscopy, specific peptide probes can be fluorescently labeled and applied in high concentration to the mucosa. The probes bind quickly, and can be imaged with a novel microendoscope, which Dr. Wang also developed.

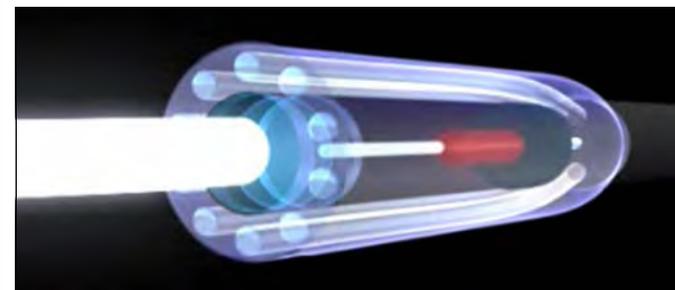
Conventional methods for *in vivo* imaging, including ultrasound, CT, MRI and PET, lack the spatial resolution and temporal speed to

capture flat lesions or lesions that may be patchy in distribution.

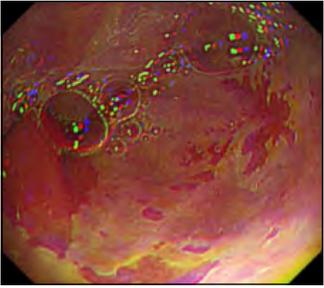
By contrast, Dr. Wang's dual-axis confocal microendoscopy platform can provide clear images of tissue in the vertical plane and detect numerous targets simultaneously. It

is being developed to perform real-time "optical biopsies" for point-of-care diagnosis.

The approach has been developed for clinical use in part through the University of Michigan Medical Procedures Unit, which is supporting early-stage clinical studies in patients to demonstrate safety and early evidence of efficacy.



Thomas Wang, MD, PhD



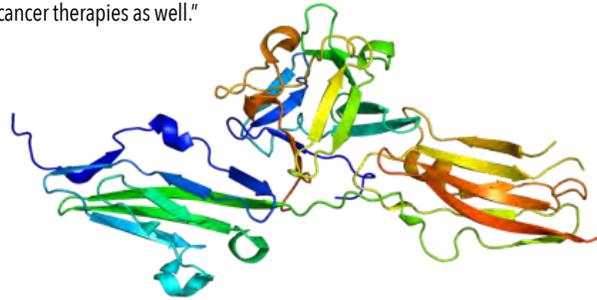
As a result of his work, Dr. Wang is widely credited with accelerating the convergence of fluorescence spectroscopy with endoscopy, and his innovations are changing existing diagnostic paradigms.

Diagnosis and staging of cancer now can be made by detecting the expression of a variety of cancer-specific molecular targets rather than on the gross visibility of lesion masses, which often aren't apparent until later stages of disease.

"The accurate diagnosis of cancer—reducing false positives and false negatives and discerning which precancerous lesions will progress in individual patients—has been a longstanding problem and requires a

creative, multidisciplinary approach," said Dr. Wang.

"Understanding the many molecular pathways involved in cancer cell proliferation coupled with peptide probes and new optical imaging approaches will help us improve the speed and accuracy of diagnosis," he added, "and if taken to the next level, will one day potentially help create a personalized approach to treatment with targeted cancer therapies as well."



## Hedgehog Signaling from Chronic Inflammation to Gastric Cancer

**JUANITA L. MERCHANT, MD, PhD**, is a molecular gastroenterologist who uses a combination of molecular tools and mouse models to dissect how chronic inflammation in the luminal GI tract alters the epithelium resulting in gastric or colon cancer.



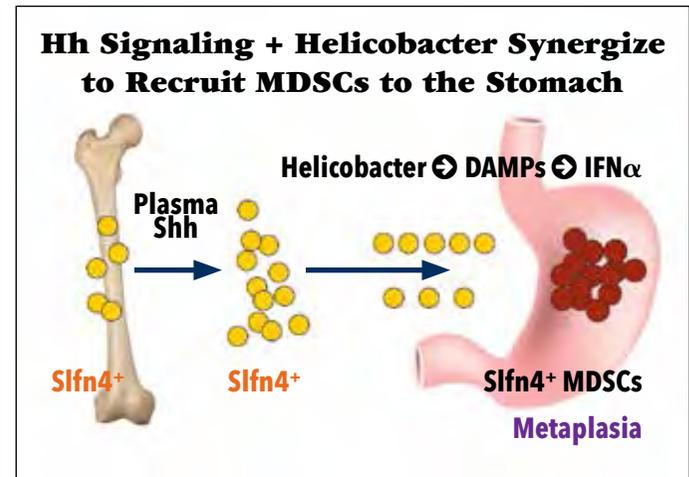
Juanita L. Merchant, MD, PhD

One of the major areas to which Dr. Merchant has made significant scientific contributions involves the role of Hedgehog signaling in

normal gastric physiology and during gastric preneoplasia. Her studies have demonstrated that the parietal cells, and therefore acid secretion, require sonic Hedgehog signaling. More recently, she has found that myeloid-derived suppressor cells (MDSCs) require Hedgehog signaling to create a permissive environment that supports the development of gastric metaplasia (Fig. 1).

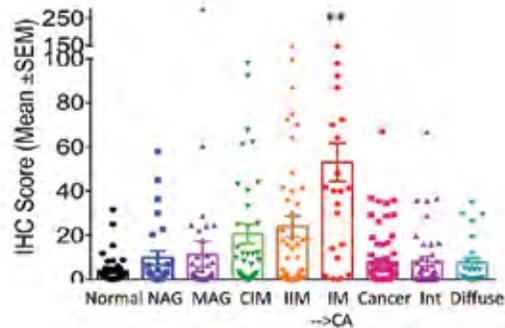
Dr. Merchant's work has identified a class of molecules called Schlafens that closely correlate with the emergence of intestinal metaplasia in mouse models and human subjects. She tested this hypothesis with a group in Spain using

a collection of specimens from their 13-year gastric cancer followup study. Their collaborative results showed that human Schlafens increase in the immune cells of patients with intestinal metaplasia who later progress to gastric cancer and suggest that Schlafens might serve as a biomarker to help clinicians decide who requires more frequent screening for gastric cancer (Fig. 2). Indeed, adding immunohistochemical detection to the pathologic diagnosis of intestinal metaplasia shifted the area under the curve (AUC). She and David Ding, MD, are currently working with UCLA CURE Digestive Diseases Research Center to identify serologic biomarkers that correlate with intestinal metaplasia.



**Fig. 1** Schlafen<sup>+</sup> MDSCs recruited to the infected stomach acquire functions that affect change in the gastric microenvironment. DAMPs = Damage-activated molecular patterns; Shh = Sonic Hedgehog. See Ding L et al *J Clin. Invest.*, 2016.

### Slfn5 Expression Decreased in Soria Cancer Samples



**Fig. 2** Slfn5 Correlates with Intestinal Metaplasia (IM), a pre-neoplastic lesion that appears in the stomach after chronic inflammation. The appearance of SLFN5 with IM correlates with a high likelihood of gastric cancer.



Dr. Deborah Gumucio

Serologic biomarkers would provide an inexpensive and easy way for clinicians to identify a subset of patients who are at high risk for gastric cancer, and the biomarkers might also serve as therapeutic targets.

Dr. Merchant is an associate director of the University of Michigan Center



Dr. Linda Samuelson

for Gastrointestinal Research (UMCGR) and serves as the co-director of the Center's Molecular Biology Core. In collaboration with **DR. DEBORAH GUMUCIO** (Department of Cell and Developmental Biology) and **DR. LINDA SAMUELSON** (Department of Molecular and integrative Physiology), Dr. Merchant successfully initiated a

Program Project on Cellular Decisions in the GI Tract (P01 DK062041).

The P01 focuses on the interplay between developmental signaling pathways, e.g., Hedgehog signaling, and environmental cues that direct cell specification, homeostasis and metaplasia, a pre-neoplastic change.

In the current funding cycle, the focus was extended to include Notch and Wnt signaling. Chronic inflammation and specifically proinflammatory cytokines play a central role in triggering patterns of cell specification during glandular transformation from a homeostatic to metaplastic state. Signals regulating the gastric stem cell were a natural extension of Dr. Merchant's seminal work in the intestine and have been extremely important in bringing together several UMCGR members.



## From Diagnosis to Cure: VIRAL HEPATITIS RESEARCH ALONG THE SPECTRUM

“Cure.” It’s a word patients long to hear, but when it comes to viral hepatitis, it has not been said often enough. **DR. ANNA SUK-FONG LOK**, the Alice Lohrman Andrews Research Professor in Hepatology, is helping to change that.

Dr. Lok, who on January 1, 2017, will become president of the American Association for the Study of Liver Diseases (AASLD), joined the U-M faculty in 1995. Over more than two decades, she has led research efforts to advance the world’s understanding of viral hepatitis, driven by a goal to reduce patient suffering and one day, she hopes, have treatments at the ready to eradicate the viruses entirely.

Dr. Lok’s research has focused on the natural history of hepatitis B and C, the role of hepatitis B virus genotypes and variants in patient outcomes and the evaluation of new treatments for both hepatitis B and C. She has been

leading an NIH-funded consortium comprising 21 adult and seven pediatric liver centers in the United States and Canada, the Hepatitis B Research Network, since 2008. She co-authored four editions of the frequently cited AASLD *Practice Guidelines on Hepatitis B*, which serve as a reference for physicians worldwide.

In a landmark study of hepatitis C, published in 2012, Dr. Lok and colleagues showed it was possible to achieve a sustained virologic response in patients infected with genotype 1 of the virus using a combination of all-oral, direct-acting antiviral agents (DAAs), rather than the standard

therapy, ribavirin and interferon (*New England Journal of Medicine*, 2012; 366:216-224).

“It was a small, proof-of-concept study,” said Dr. Lok, “but showing that what all our patients had been hoping for (a cure without having to take injections for a year that make them sick) can happen was astounding. An editorial accompanying that article was aptly titled ‘A Watershed Moment in the Treatment of Hepatitis C.’”

Dr. Lok now is investigating different combinations of DAAs that might further shorten treatment and improve cure rates for additional virus geno-

types as well as among patients with advanced liver disease and those who have failed prior treatment.

But the breakthrough can only benefit patients if treatment is initiated early; therefore, improved screening is critical. Dr. Lok recently conducted a pilot study using U-M Health System electronic medical records system to identify patients born between 1945 and 1965—a generation with a much higher prevalence of infection—who have not yet been screened. The system alerts patients’ primary care physicians and links to an order set and educational materials. The pilot improved screening rates sevenfold and has been rolled out to primary care providers throughout the UMHS system.

Typical hepatitis C with dense lymphocytic inflammation

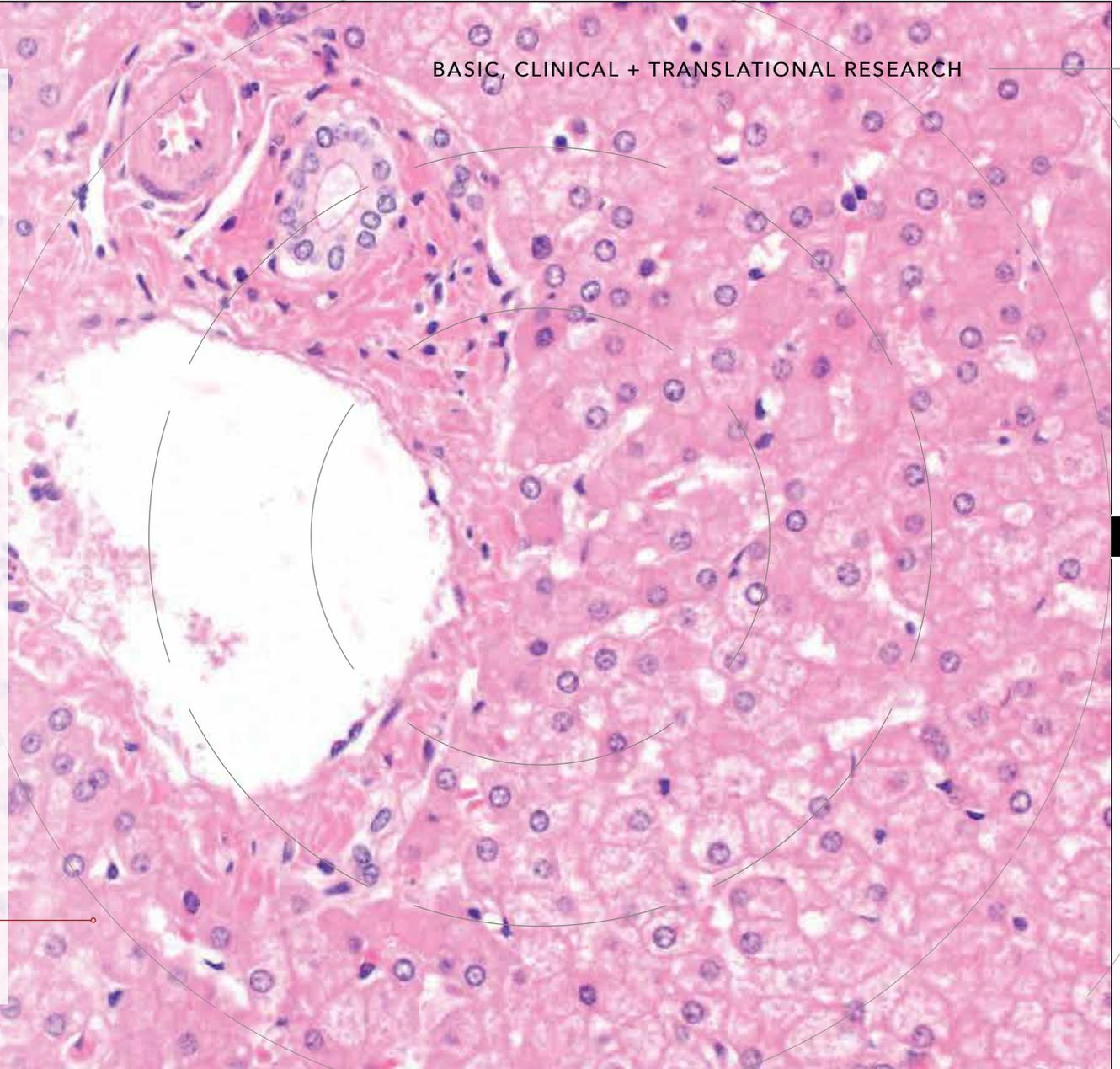
Continuing along the spectrum, Dr. Lok developed a noninvasive way to stage liver damage that results from hepatitis C infection. This alternative to liver biopsy assesses fibrosis and cirrhosis using two measures obtained from a simple blood test: platelet count and aspartate aminotransferase (AST) (*Hepatology*, 2003; 38(2):518-26). The AST-to-platelet ratio index (APRI), has been adopted by the U.S. Centers for Disease Control and Prevention and the World Health Organization as a simple and accurate method to assess stage of liver damage, not only for those with hepatitis C but also for individuals with hepatitis B.

To assess the likelihood of progression to advanced liver disease in patients, Dr. Lok also partnered with colleagues

to use advanced statistical methods to develop dynamic predictive models. In addition to baseline data, the models incorporate longitudinal patient information. Risk calculations adjust as the individual's course of disease changes.

"My patients continue to guide me toward the research questions we need to be asking and to persevere when we hit roadblocks," said Dr. Lok. "Seeing my own patients and knowing patients all over the world get better as a result of the knowledge we've gained from our work is the biggest reward a researcher can ever ask for."

Recovering from hepatitis C treatment:  
returning to normal liver histology



## Promising Targets for New IBS Treatments: GUT DYSBIOSIS AND MUCOSA PERMEABILITY IMPAIRMENT

Irritable bowel syndrome (IBS) is one of the most common GI disorders we encounter in our practice. Worldwide, approximately 10 to 20 percent of adults have symptoms consistent with IBS. Advances in basic, mechanistic and clinical investigations have improved our understanding of this disorder and its physiological and psychosocial determinants. Altered GI motility, visceral hyperalgesia, disturbance of brain-gut interaction, abnormal central processing, autonomic and hormonal events, genetic and environmental factors and psychosocial disturbances are veritably involved, depending on the individual. This progress may result in improved methods of treatment.

At the University of Michigan, **CHUNG OWYANG, MD** has assembled a group of basic and clinical investigators with diverse expertise to unravel the puzzle of IBS, including neurogastroenterologists, mucosa biologists, microbiome investigators and genomic scientists; the program has an annual research base of \$1.8 million in National Institutes of Health funding. At U-M, an IBS registry and biosamples repositories for blood, fecal samples and colonic tissues will capitalize on advances in genomic,

proteomic and system biology to promote translational research.

### Mucosal Biology Research

Recent clinical studies indicate that most IBS patients have clinical mucosal inflammation with activated mast cells, lymphocytes and enhanced expression of pro-inflammatory cytokines. These abnormalities may compromise epithelial integrity and lead to visceral hypersensitivity. This series of events provides potential

therapeutic targets for intervention. **DR. ASMA NUSRAT** from the Department of Pathology, a key member of U-M's Center for Gastrointestinal Research (UMCGR), has a longstanding research interest directed at understanding basic mechanisms for intestinal epithelial barrier regulation and repair during inflammatory states in the gut. She collaborates closely with her colleague, **DR. CHUCK PARKOS**, Chair of the Department of Pathology, who has had a career-long

interest in elucidating mechanisms guiding neutrophil trafficking across the intestinal epithelium.

**DR. GABRIEL NUNEZ**, also from the Department of Pathology, examines the role of gut microbiota in the regulation of the gut immune system which is abnormal in IBS patients. The group also includes **DR. JOHN WILEY**, a neurogastroenterologist, who is interested in investigating the role of epigenetic pathways in stress-induced visceral hyperalgesia. "We believe epigenetic targets may play a significant role in how IBS patients perceive pain," said Dr. Wiley, who is looking at the histone-regulated pain pathways that carry signals from the viscera, through the spinal cord, to the brain.

### Gut dysbiosis in IBS

In recent years it has become apparent that gut dysbiosis is common amongst IBS patients. It is conceivable that abnormalities in gut microbiota act in concert with environmental factors to alter epithelial permeability allowing access of luminal toxins into the mucosa, which may in turn cause degranulation of mast cells. The release of histamine, proteases and prostaglandins may act on enteric neurons and gut muscles to produce symptoms of IBS. Hence, normalizing microbiota in the gut may be an attractive therapeutic target to treat IBS. This can be achieved through diet or by the use of probiotics or antibiotics.

Currently the cause of gut dysbiosis in IBS is unknown. Dr. Owyang

has assembled a premier group of microbial investigators such as **DRS. VINCENT YOUNG, NOBU KAMADA, JOHN KAO** and **MERRITT GILLILLAND** to investigate whether dysbiosis may be related to stress and/or diet. It is also unclear if further microbial changes are causal, consequential or merely the result of change in bowel habit. Furthermore, these investigators, in collaboration with Drs. Owyang and Wiley, examine how gut microbiota modulate gut-brain interaction. In collaboration with **DR. CHUCK BURANT**, these investigators also examine the role of bacterial metabolites and signaling molecules in communicating with the host systems, such as the enteric nervous system and the brain.

**Biomarkers and targeted treatments**

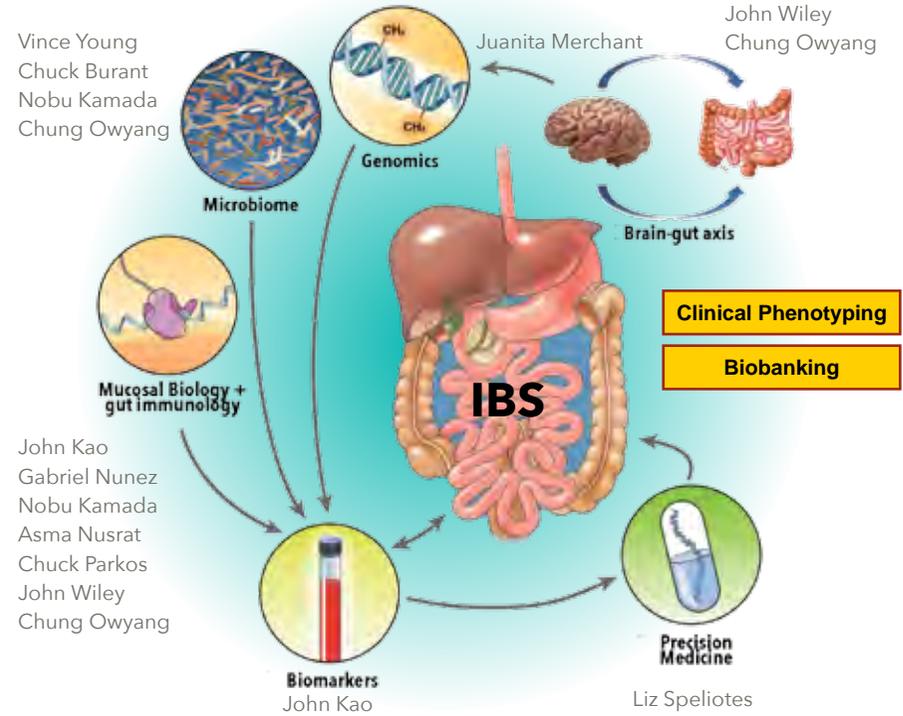
Dr. Kao and his laboratory have a long-established interest in looking for biomarkers for gut dysbiosis. Clinically, this is important for identifying subsets of IBS patients who may be more responsive to modulation of gut dysbiosis. In a recent study, Dr. Kao and researchers in his lab found that the majority of post-infectious IBS patients with gut dysbiosis have elevated mucosal Duox2 levels. Ongoing work will further validate the usefulness of measuring colonic mucosa Duox2 levels to identify antibiotic-responsive IBS patients.

In a subset of IBS patients, there may be genetic abnormalities affecting the serotonin synthetic and transport pathways. **JUANITA MERCHANT, MD,**

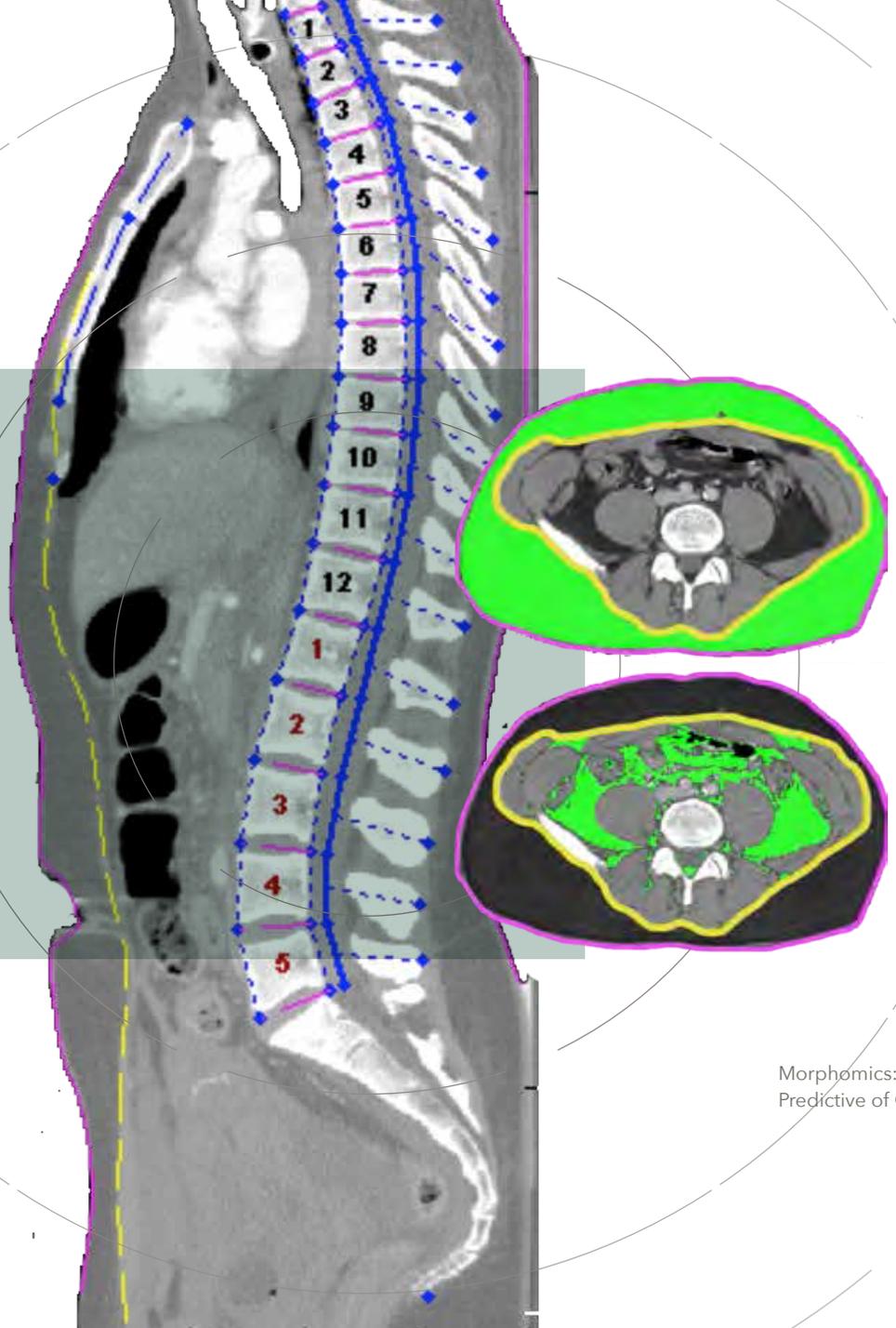
**PhD**, a molecular biologist, recently identified a functional tryptophan hydroxylase 1 (TPH-1) polymorphism associated with IBS-diarrhea predominant. This may help to predict IBS patients' response to medications targeting the serotonin signaling system including the recently developed TPH-1 antagonist.

Using a multidisciplinary approach, Dr. Owyang and his colleagues are making great strides to understand the complexity of IBS and identify specific causes that may result in improved methods of treatment. "The discovery that gut dysbiosis and impaired permeability occur in IBS offers new promising targets for treatment," he said. This may pave the way to practice precision medicine in treating IBS, a program directed by **DR. LIZ SPELIOTES**.

**Solving the Puzzle of IBS**



NIH FUNDING = \$1,844,565/YR



### Inflammatory Bowel Disease Research at the Forefront

The University of Michigan Inflammatory Bowel Disease program is a research leader in this rapidly changing field. The program has strong research funding coming from a variety of sources, including the National Institutes of Health, Department of Defense, U.S. Department of Veterans Affairs and Crohn's and Colitis Foundation (CCFA).

#### Basic Science Research in IBD

**RYAN STIDHAM, MD, MSc** is leading proteomic studies in patients with Crohn's disease to identify novel biomarkers that can detect and monitor progression of intestinal strictures. The laboratory of **PETER HIGGINS, MD, PhD, MSc**, works on the mechanisms of intestinal fibrosis to identify targets for anti-fibrotic drug development. Dr. Higgins uses human intestinal organoids as a model for the intestinal scarring in Crohn's disease to test promising therapies. **SHRINIVAS BISHU, MD** studies the role of the interleukin-17 and interleukin-23

pathways in the inflammation of IBD. **JOHN KAO, MD**, focuses on the role of dendritic cells in sampling the gut microbiome, and T regulatory cells in damping the inflammatory response. **NOBU KAMADA, PhD**, studies the interaction between the gut microbiota and the human gut immune system.

#### Translational Research in IBD

Dr. Higgins and **AKBAR WALJEE, MD, MSc**, in collaboration with statistics faculty, are developing machine learning algorithms to predict the response of IBD patients to thiopurines and biologic therapies with the support of a National Institutes of Health (NIH)

R01 award. Dr. Stidham, in collaboration with radiologists and computer scientists, is developing algorithms to rapidly analyze CT scans in IBD patients to identify abscesses, reproducibly measure inflammation and detect strictures with the support of a Department of Defense grant.

Dr. Higgins' lab, with the support of the Michigan Center for Therapeutic Innovation, has identified candidate antifibrotic medications and demonstrated their effect on human intestinal cells and human organoids; they are now testing these new drugs in animal models. Dr. Higgins is also collaborat-

Morphomics: Objective Fat Assessment Predictive of Complications in IBD

ing with the U-M Microbiome Core to study the role of the microbiota in flares of ulcerative colitis, and the importance of reconstitution of the gut microbiota after *Clostridium difficile* infection and antibiotic therapy, with the support of a CCFA grant. The Michigan IBD Biobank provides a platform for basic scientists to obtain biopsies, cells and serum from IBD patients to test new hypotheses about the mechanisms of inflammatory bowel disease.

#### Clinical Research in IBD

Dr. Higgins, in collaboration with radiology faculty, has developed new methods of shear wave velocity ultrasound to measure the stiffness of strictures in the intestine in Crohn's disease. Their NIH R01-supported research will measure the stiffness of strictures

in patients over time to determine whether obstruction and surgery can be predicted.

Dr. Waljee has developed a machine learning algorithm to identify IBD patients at risk for flare in the next six months based on data in the Veterans Administration electronic medical record, to provide an opportunity for intervention. **SHAIL GOVANI, MD, MSc**, studies the importance of adherence to subcutaneous biologic therapies in IBD, and has found that missing only a few doses has a significant effect on long-term outcomes. He is developing interventions to improve patient adherence to subcutaneous biologic therapy in IBD.

Dr. Higgins' group has identified five factors in the electronic medical record

that predict which patients are at risk for Emergency Department visits, hospitalizations and high charges in the next year. Interventions are planned for these high-risk patients to prevent such events and provide high value care.

In addition, our IBD group has collaborated with Lycera, a local startup on U-M's North Campus, which has developed a new, gut-specific therapy for ulcerative colitis that has entered a phase 2 clinical trial. The University of Michigan IBD clinical trials group has five full-time study coordinators and over 50 IRB-approved clinical studies. They have recently participated in the trials supporting the approval of Vedolizumab and Ustekinumab, and continue to offer many other new options to our patients with IBD.



Shear Wave Velocity Imaging

## Epigenetic Pathways in Stress and Abdominal Pain

Chronic stress is associated with enhanced abdominal pain, particularly in patients with functional GI disorders such as irritable bowel syndrome (IBS). Recent evidence suggests that altered gene expression involving epigenetic regulatory pathways may play an important role in understanding why this may be.

The research of **JOHN W. WILEY, MD**, focuses on pain pathways that innervate the gut and how these pathways are altered in diabetes mellitus, in the aging process and under conditions of chronic stress. His laboratory has identified specific changes in the regulation of ion channels located on the sensory nerves that transmit pain signals from the colon in diabetic rodent models, in aged animals and in models of chronic stress. His recent research is investigating the role of epigenetic regulatory pathways in chronic stress-associated enhanced abdominal pain.

"It may be a bold statement, but we are in the midst of a renaissance in how we understand the ways in which gene transcription occurs," said Dr. Wiley. "Since the Human Genome Project, we as a scientific community have been realizing that we didn't know as much as we thought we did about how individuals differ from one another."

Enter the field of epigenetics: the variety of heritable, potentially reversible processes that regulate gene activity and expression, independent of actual changes in DNA sequence. An understanding of epigenetics is critical to

explaining a large amount of variation in heritable traits and disease risks as well as therapeutic responses and the risk of side effects.

Epigenetic changes occur primarily through several mechanisms, including DNA methylation by DNA methyltransferases (DNMTs), which tends to inhibit gene transcription, and DNA demethylation, which typically inhibit gene transcription. DNMTs are a popular target in cancer research.

In addition, non-coding microRNAs also tend to inhibit gene expression. MicroRNAs in particular represent potential new disease biomarkers and



John W. Wiley, MD

therapeutic targets. Histone modifications represent yet another mechanism, and these usually promote gene transcription. When DNA is tightly wound around histones, genes are not accessible to be transcribed. When certain molecules attach to the histone tails, however, they open up and DNA can be transcribed.

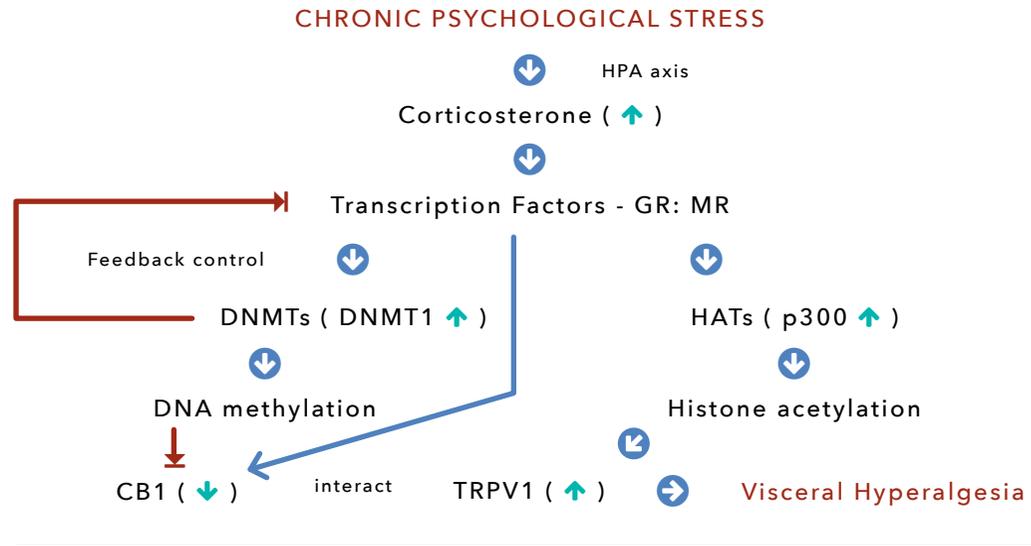
Clinically, patients with IBS experience both abdominal pain and a change in bowel habits. Dr. Wiley's laboratory is investigating how pain transmission occurs and the role of epigenetic pathways in modifying the genes that regulate pain.

"We believe epigenetic targets may play a large role in how IBS patients perceive pain," said Dr. Wiley, who is looking at the histone-regulated pain

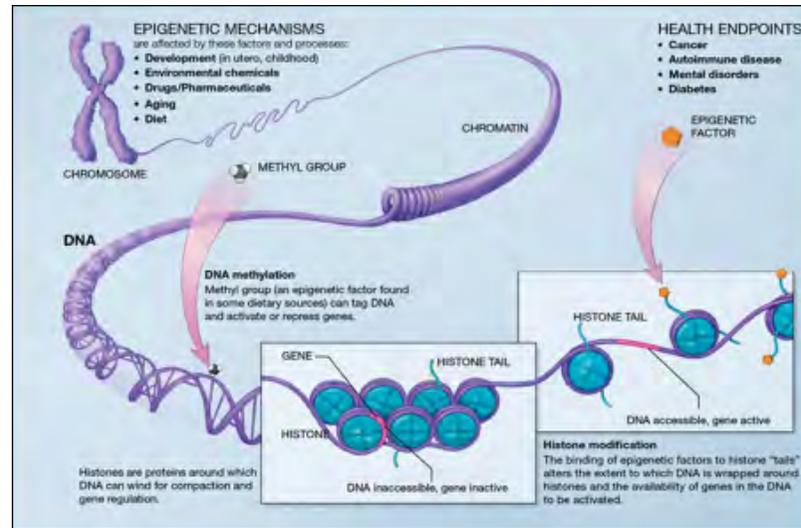
pathways that carry signals from the viscera, through the spinal cord to the brain. Subsets of neurons in the spinal ganglia carry only pain signals, and his lab is investigating whether histone-regulated pathways are differentially expressed in those nerves.

In work published in *Gastroenterology* in 2015 (Jan;148(1):148-157.e7), Dr. Wiley and collaborators measured pain activation and used molecular probes to look more closely at epigenetic pathways involved in the enhanced perception of pain. Targets included a common target in pain research, transient receptor potential vanilloid type 1 (TRPV1), and the endogenous cannabinoid receptor 1 (CNR1) to better understand how it might inhibit pain perception.

### Epigenetic regulation of chronic stress-induced visceral hyperalgesia (HONG ET AL. GASTRO., 2015)



## Epigenetic Mechanisms

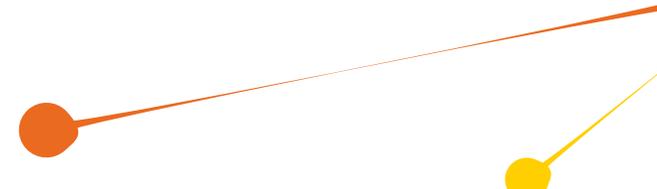
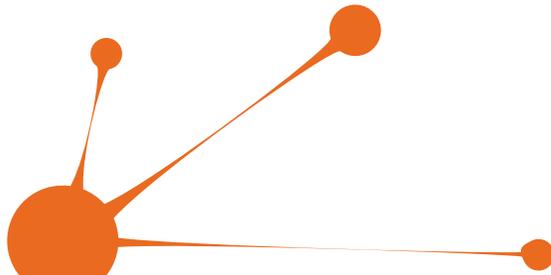


The research found that mice subjected to stress showed features similar to those in human IBS and that the anti-pain pathway was inhibited in our model through methylation, while the pain activation pathway in the model was turned on through a process of histone acetylation. "In a very important pathway modulating pain, you have both systems—well studied—included in the net outcome of pain perception," he said.

The research also found that expression of these pathways was region-specific along the spinal cord, limited to the centric pathways going out to the viscera. Expression of these pathways was not present in, for example, the sciatic nerve distribution down the leg.

The work is leading to additional areas of inquiry, including the role of epigenetic pathways involved in modulating intestinal barrier function along the paracellular route. "We know these targets are altered in cancer, but we know very little about how epigenetic pathways may modify the expression of these and other types of junctions in the non-malignant milieu," said Dr. Wiley.

With his interest in stress, Dr. Wiley looked at its targets, including glucocorticoid receptors, which act as a major transcription factor in the body. His team compared the expression of the glucocorticoid receptors in the colon and jejunum and found it was orders of magnitude higher in the colon.



"Ultimately stress is mediated through these receptors, which might explain why we see such region-specific differences in the model and indeed, we believe, in humans," he said.

Now Dr. Wiley is looking at the expression of epigenetic regulatory pathways in colon crypts, and "seeing some very interesting differential expression of these DNMTs," he said. "That's prompting us to take the story from dorsal root ganglion neurons to the intestinal tract."

The story is an evolving one, and Dr. Wiley is furthering the work using super-high-resolution microscopy, which provides resolution down to about 20 nanometers. "We can actually see DNA forming loops using this technology," he said, "and it's these loops that allow

intron regions to interact with promoter regions and modify gene expression."

Combine such high resolution technology with bioinformatics and "the story about how epigenetics differentially affects gene expression continues to unfold in some very intriguing ways," Dr. Wiley said.



## Precision Medicine:

### UNRAVELING THE CAUSES OF OBESITY AND LIVER DISEASE THROUGH GENOMIC RESEARCH

More than one-third of the U.S. population and over one billion individuals worldwide suffer from obesity. Some go on to develop related metabolic diseases, such as diabetes, heart disease or nonalcoholic fatty liver disease (NAFLD). NAFLD develops when fat is deposited in the liver, and it is projected to be the most common liver disease globally by 2020. NAFLD can progress to nonalcoholic steatohepatitis and cirrhosis and has also been associated with development of other metabolic complications such as cardiovascular disease.

But not all people who are obese develop complications from obesity, and those who do don't develop the same complications. Similarly, not all individuals who deposit fat in their liver will go on to develop advanced liver disease or related metabolic complications.

"Our understanding of the etiology of these diseases is very poor, and thus few effective treatments exist," said **ELIZABETH SPELIOTES, MD, PhD, MPH**, associate professor in the departments of Internal Medicine and Computational Medicine and

Bioinformatics. "Given the epidemic proportions of obesity and NAFLD, these are some of the biggest unmet medical needs of our time. Better defining the causes of these diseases will allow us to develop precision care for these patients—getting the right treatment to the right patient at the right time—to actually cure what ails them," she said. "If we understand the biology of the disease, we can define an individual's risk of developing it, and we can develop tailored and effective therapeutic approaches with fewer side effects."

Dr. Speliotes, who received the University of Michigan 2016 Dean's Award for Basic Science Research, works to untangle the genetic and environmental influences that predispose individuals to obesity and NAFLD. Her goal is to translate the findings into improved diagnosis, management and treatment of these conditions.

#### Gaining new biological insights

Both obesity and NAFLD are complex genetic traits, meaning they result from a combination of genetic and

environmental factors. To better understand our susceptibility to these diseases she carried out the largest genome-wide association studies for obesity and NAFLD.

In a paper published in *Nature* in 2015 (Feb 12; 518 (7538):197-206), Speliotes and colleagues reported their identification of 98 genomic loci for body mass index (BMI), a measure of obesity that influences its development, in more than 340,000 individuals. Many of the genes implicated in obesity are expressed in the nervous system, which was not expected for a metabolic disease.

Indeed some of the most enriched regions include genes that play roles in learning, memory, smell and emotion in addition to genes that, as

expected, affect feeding and satiety, energy expenditure and insulin biology.

"Based on the fact that we are able to map these genetic signals to the brain suggests a biological cause to obesity as opposed to pure willpower as the cause, as some have suggested," Dr. Speliotes said. "And since most of these genes were completely novel, the findings suggest that we have much to learn from further study about our susceptibility."

Dr. Speliotes and colleagues also carried out similar analysis for NAFLD, identifying five variants associated with NAFLD that explain between 17 and 20 percent of trait heritability (*PLoS Genetics*, 2011; 7(3): e1001324). These variants implicate

genes involved in glucose and lipid metabolism as being causal to this disease.

"There's been a longstanding debate in hepatology about whether steatosis is benign. The genetics are telling us that lipid metabolism is causally related to NASH and fibrosis, so so-called benign disease in the liver may not be so benign after all. The days of waiting to see if fat in the liver will develop into cirrhosis before we treat it may soon be over," Dr. Speliotes said.

#### Clinical prediction

The variants that affect BMI individually have small effects, with the largest at obesity-associated (FTO) gene conferring an increased odds ratio of developing obesity of 1.25. While odds ratios suggested

the individual variants are not that predictive, the cumulative effects of the variants *are* medically significant. Individuals carrying the most BMI-increasing variants (top 5 percent) are on average 9 to 11 kilograms heavier than those carrying the least (bottom 5 percent). Gaining or losing 9 to 11 kg can lead to development or amelioration of diabetes, for example, in a single individual.

The odds ratios of the NAFLD-associated variants per allele for predisposing to advanced liver disease, such as NASH/fibrosis were higher than in the BMI work, however -- between 1.37 and 3.26 per allele. Such an increased risk is medically significant for individuals who carry them and may soon merit individualized treatment

recommendations. Indeed, since most people that have NAFLD do not know they have it, and since this disease was not even defined as a disease until about 10 years ago, "genetic profiling may give clinicians a rapid way to identify patients at high risk of developing NAFLD," said Dr. Speliotes.

#### Defining subtypes of disease

For both obesity and NAFLD, Speliotes and colleagues have found that some of the variants that predispose to these conditions increase risk of related metabolic disease or advanced liver disease as expected epidemiologically. This begins to define the common genetic susceptibility to developing these diseases.

Interestingly however, the investigators have also identified the variants that



Elizabeth K. Speliotes, MD, PhD, MPH

predispose to obesity or NAFLD that protect from development of related metabolic diseases, such as diabetes or cardiovascular disease. These can provide insights into how to dissociate these conditions and thus even treat metabolic disease in obese individuals. These genetic variants are also now helping them to define subtypes of NAFLD that may help to explain why only some develop related metabolic diseases while others do not.

**Defining tailored treatments for disease**

Dr. Speliotes' work is identifying specific gene targets for therapeutic intervention and suggesting new approaches to treatment. "The genes implicated from these studies not only define subtypes of disease but

suggested how we can correct the defects seen by altering their function," she said.

Further, the findings indicate that when most genes are severely perturbed they will disrupt multiple traits, suggesting that medications that target these genes will have side effects.

"Nature has weakly changed the function of these genes to allow for human variation to occur while minimizing the detrimental side effects of drastic changes to gene function. This suggests that if we can use medicines to weakly increase or decrease the effects of identified genes to converge on affecting the desired trait like fatty liver but not converge on their effects on unrelated biologies, we can increase the on target effects of that

medicine combination and minimize side effects."

Dr. Speliotes and colleagues have further identified environmental and biological factors that interact with these genetic changes to exacerbate development of disease. Certainly, those at high genetic risk of developing NAFLD who carry particular genetic variants can be counseled as to what to avoid to prevent development of the disease.

In these ways, Dr. Speliotes is helping to define the underlying etiologies of these heterogeneous diseases and use them to better define disease subtypes and match them to new therapies, so that we can have more effective treatments for these conditions in the future.





BASIC, CLINICAL + TRANSLATIONAL RESEARCH

## Collaboration: JOINT APPOINTMENTS

### Collaboration with Basic Science Departments

One of the consummate strengths of our GI Division is its cross-disciplinary approach to research, exemplified by the many joint faculty appointments within other basic science departments. Among these we have seven faculty from the Department of Molecular and Integrative Physiology (MIP) who also hold appointments in the Division of Gastroenterology and Hepatology.

**BISHR OMARY MD, PhD**, is Professor and Chair of the Department of Molecular & Integrative Physiology and the H. Marvin Pollard Professor of Gastroenterology. His research focuses on investigating the cytoskeletal intermediate filament proteins that are specifically expressed in digestive-type



epithelia, understanding the molecular pathogenesis and significance of the hepatocyte inclusion bodies and defining potential therapeutic targets for acute and chronic hepatitis. Since joining the University of Michigan in 2008 Dr. Omary has worked closely with the Division to enhance its research and education missions, and serves as an Associate Director of the U-M Center for Gastrointestinal Research (UMCGR) and co-director of the Center's Protein Localization,

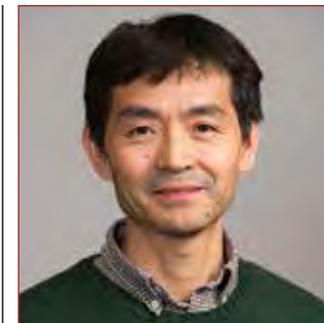
Identification and Folding Core. He is also co-principal investigator in the GI Division's NIH T32 Basic and Translational Sciences Training Grant. As Editor and Chief of *Gastroenterology* (2011 to 2016), Dr. Omary interacted closely with many GI faculty members who served on the editorial board.

**LINDA SAMUELSON, PhD**, is the John A. Williams Collegiate Professor of Gastrointestinal Physiology and Professor in the Department of Molecular & Integrative Physiology. Dr.



Samuelson's research focuses on Notch pathway regulation of epithelial cell homeostasis through modulation of gastrointestinal stem cell function. Dr. Samuelson has a joint appointment in the Division of Gastroenterology and Hepatology. In 2002, she collaborated with Drs. Merchant and Gumucio to initiate a program project (P01 DK062041) to investigate the interplay between developmental signaling pathways and environmental cues. Dr. Samuelson is a key member of the Michigan Center for Gastrointestinal Research (UMCGR), serving as co-director of the Molecular Biology Core. She also co-directs the PhD predoctorate mentoring of the Division's T32 grant in Basic and Translational Research Training.

**LIANGYOU RUI, PhD**, is a professor in the Department of Molecular & Integrative Physiology. Dr. Rui investigates the physiological and



molecular mechanisms of obesity, diabetes and nonalcoholic fatty liver disease (NAFLD). Dr. Rui has a joint appointment in the Division of Gastroenterology and Hepatology and works closely with Dr. Owyang to investigate the hypothalamic neurocircuits in the regulation of energy metabolism. Dr. Rui is a key investigator of the UMCGR investigating neurobiology in appetite control, metabolism and pain.



**JOHN WILLIAMS, MD, PhD** is the Horace W. Davenport Collegiate Professor of Physiology and Professor in the Department of Molecular & Integrative Physiology. Research in Dr. Williams' laboratory focuses on the regulation of pancreatic function by hormones and neurotransmitters. Dr. Williams has been a member of the UMCGR since its inception and served as an associate director of the Center. He also directs the original morphology core, which has now evolved to the

Protein Localization, Identification and Folding Core, where he currently serves as Core Associate Director. His expertise in cell biology, calcium imaging studies and pancreatic physiology serve as an important resource to Center members who are conducting research using these technologies.

**YATRIK SHAH, PhD**, is an associate professor in the Department of Molecular & Integrative Physiology. The major goal of his research program is to determine the molecular mechanisms



by which oxygen sensing transcription factors regulate gastrointestinal homeostasis, inflammation and cancer. Dr. Shah has been a key investigator of the UMCGR and is an emerging mucosal biology research leader. Over the years, he has collaborated with several GI Division faculty members such as Dr. John Kao and Dr. Juanita Merchant on pathways related to mucosa inflammation.

**HOWARD CRAWFORD, PhD**, is a professor in the Department of



Molecular & Integrative Physiology and holds a joint appointment as Professor in the Department of Internal Medicine, Division of Gastroenterology and Hepatology. In addition to overseeing a robust research program aimed at understanding molecular pathways in pancreatic adenocarcinoma and pancreatitis, Dr. Crawford serves as Director of the Pancreas Research Program in the Departments of Medicine and Molecular & Integrative Physiology, and as Director of the Genetically Engineered Mouse Models of the Pancreatic Cancer Core in the Translational Oncology Program and the Cancer Center. Dr. Crawford collaborates frequently with many investigators of the UMCGR, including Andy Rhim MD, Marina Pasca Di Magliano PhD and Eric Fearon, MD, PhD.

**COSTAS LYSSIOTIS, PhD**, is an assistant professor in the Department



of Molecular and Integrative Physiology with a joint appointment in the Division of Gastroenterology and Hepatology. His lab studies the biochemical pathways and metabolic requirements that enable tumor survival and growth and how this information can be used to design targeted therapies. Dr. Lyssiotis collaborates with many members of the UMCGR, including Andy Rhim MD, Marina Pasca Di Magliano PhD, and Howard Crawford, PhD.



**DEBORAH GUMUCIO, PhD**, is the James Douglas Engel Collegiate Professor in the Department of Cell and Developmental Biology. Current research interests in Dr. Gumucio's laboratory include investigating the role of the hedgehog pathway in gut inflammation and in villus formation. A longtime investigator at UMCGR, she collaborated with Drs. Merchant and Samuelson in 2003 to initiate a program project, P01 DK062041, to investigate the interplay

developmental signaling pathways and environmental cues that regulate epithelial homeostasis. Dr. Gumucio also plays a critical role as part of the Center Mucosal Biology Group, collaborating with other investigators such as Jason Spence, PhD, and Andrea Todisco, MD. She mentors other faculty members such as Michelle Muza-Moons, MD, PhD.

**Joint Appointment of GI Faculty in Basic Science Departments**

**CHUNG OWYANG, MD**, is the H. Marvin Pollard Professor of Internal Medicine and Chief of the Division of Gastroenterology and Hepatology. He holds a joint appointment as Professor of Molecular and Integrative Physiology. Dr. Owyang's research interests focus on neurohormonal control of digestive functions including pancreatic, endocrine and exocrine function, GI motility and pain behavior. In his role as the Chief of the Division



and Director of the UMCGR, he works closely with many members of the Department of Molecular and Integrative Physiology (Drs. Omary, Williams, Samuelson, Rui) and Drs. Nunez and Nusrat from the Department of Pathology. Together with Dr. Omary, they jointly direct the Division's T32 grant in basic and translational sciences.

**JUANITA MERCHANT, MD, PhD**, is the H. Marvin Pollard Professor of Gastrointestinal Sciences in the



Department of Internal Medicine, with a joint appointment as Professor in the Department of Molecular and Integrative Physiology. Dr. Merchant's research focuses on the molecular mechanisms underlying normal and cancerous epithelial cell growth in the luminal gastrointestinal tract. Over the years, Dr. Merchant has worked closely with her basic science department colleagues such as Drs. Gumucio and Samuelson to initiate a P01 program project to study cellular decisions in the

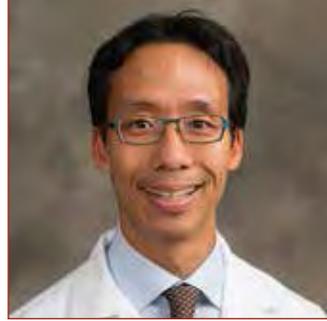
GI tract. Together with Dr. Samuelson, she also directs the Molecular Biology Core of the UMCGR. In addition, she serves as an associate director of the UMCGR. In 2008, Dr. Merchant was inducted into the prestigious Institute of Medicine (now the National Academy of Medicine).

**JOHN CARETHERS, MD**, is the John G. Searle Professor and Chair in the Department of Internal Medicine and Professor in the Department of Human Genetics. Dr. Carethers is a key



investigator at the Michigan Center for Gastrointestinal Research and collaborates closely with Eric Fearon, MD, PhD, on the TGF beta signaling pathway; John Williams, MD, PhD and others on the study of intracellular calcium stores and activation of PCK alpha; and Linda Samuelson, PhD, on the development of transgenic mice to study a variety of genetic and epigenetic events that may result in the growth and progression of colon cancer. In 2012, Dr. Carethers was inducted into the National Academy of Medicine.

**ANDREW TAI, MD, PhD**, is an assistant professor in the Department of Internal Medicine, Division of Gastroenterology and Hepatology with a joint appointment as Assistant Professor in the Department of Microbiology and Immunology. Dr. Tai's research concentrates on the molecular virology of hepatitis C virus,



and more recently his laboratory has begun working on the molecular virology of dengue virus, with a focus on identifying and characterizing host-pathogen interactions. Dr. Tai has been a productive member of the UMCGR since 2008 and actively collaborates with other virology-focused investigators in the basic science departments.



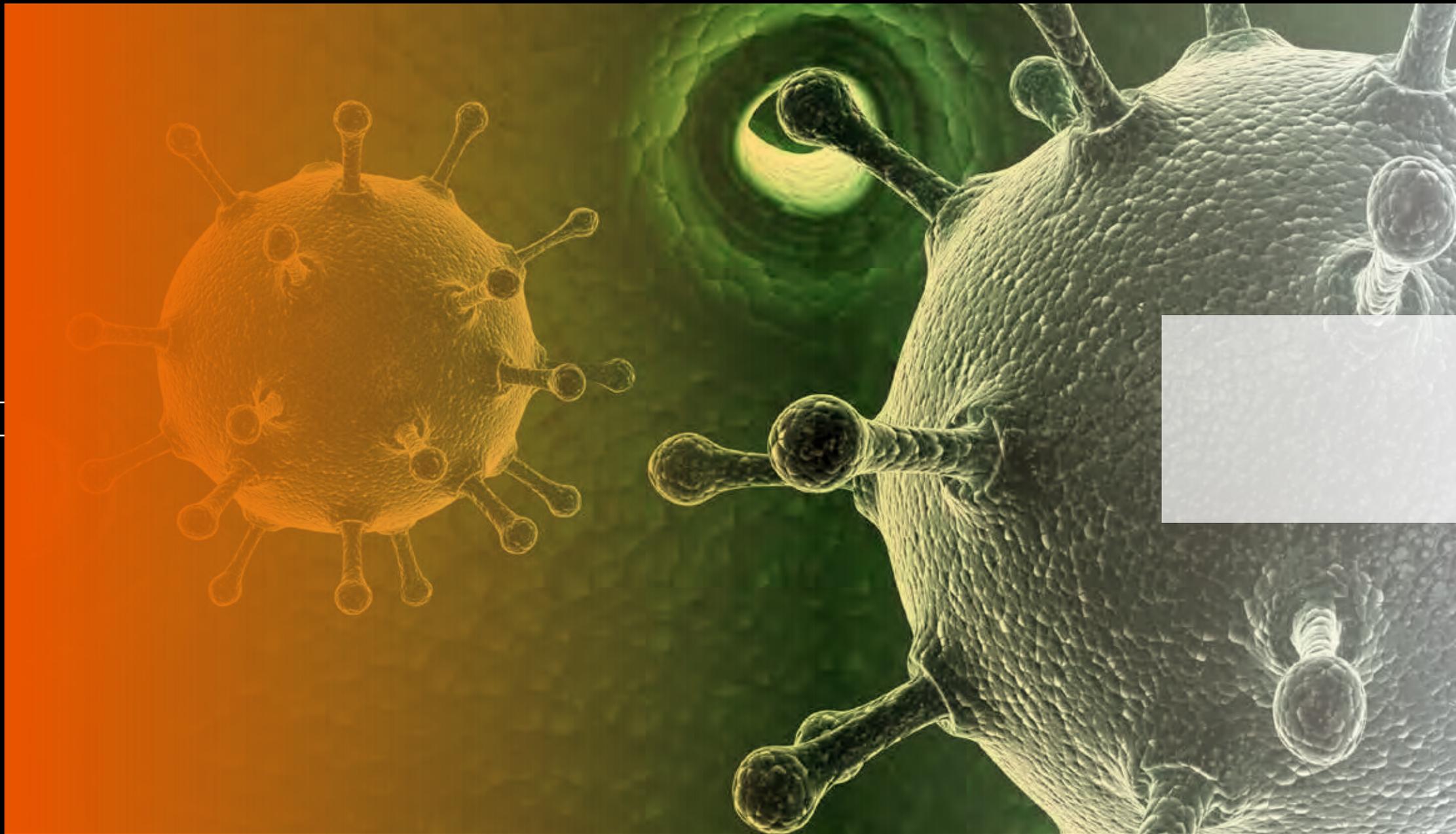
**ELIZABETH SPELIOTES, MD, PhD, MPH**, is an associate professor in the Department of Internal Medicine, Division of Gastroenterology and Hepatology with a joint appointment as Associate Professor in the Department of Computational Medicine and Bioinformatics. Dr. Speliotes' research group utilizes human population based and functional genetic studies to define and characterize causes of human obesity, nonalcoholic liver disease (NAFLD) and related metabolic diseases

so that they can develop better ways to prevent, diagnose and treat them. She is a key investigator at the UMCGR and collaborates frequently with members of other basic science departments including Jiandie Lin, PhD and Charles Burant, MD, PhD.

**THOMAS WANG, MD, PhD**, is the Marvin A. Pollard Collegiate Professor of Endoscopy Research with a joint appointment as Professor of Biomedical and Mechanical Engineering. Research in Dr. Wang's Laboratory concentrates



on molecular imaging in the digestive tract and emphasizes the development and validation of novel molecular imaging methods and systems for early detection of disease. Dr. Wang's collaborative group focuses on cutting-edge translational research that connects U-M's College of Engineering and Medical School. Dr. Wang has been a productive and active member of the UMCGR and a driving force in many of the Center's translational and clinical studies. For example, he designed an endoscopic laser confocal fluorescence microscope, which provided real-time histology with a fluorescently labeled peptide during endoscopy. Images show differences between human squamous, metaplasia and dysplasia mucosa. This first in-humans study provides groundbreaking endoscopic research technologies showing that confocal endomicroscopy can guide tissue biopsy and early dysplasia detection.





## **Global Reach:** ENGAGING WITH THE WORLD



## Global Impact:

IMPROVING GI HEALTH, HEALTHCARE AND TRAINING WORLDWIDE

"Global initiatives are essential to our academic mission," said **JOSEPH KOLARS, MD** (Fellowship 1989), who holds the Josiah Macy, Jr., Professor of Health Professions Education in the Division of Gastroenterology and Hepatology. "Global initiatives are crucial to enhancing opportunities for education, research and innovation, and to improving health and reducing the burden of disease worldwide."

The Division has been active across borders for many years, dating back to the 1980s under the leadership of then-Division Chief **TACHI YAMADA, MD, KBE**. Dr. Yamada expanded the international dimension of the Division's work, particularly with Japan, increasing exchanges among learners and teachers at U-M and abroad. Many of Dr. Yamada's former Japanese trainees have gone on to become leaders in gastroenterology. Dr. Kentaro Sugano is the Chair of Medicine at Jichi Medical University in Japan, and Dr. Tsutomu Chiba is now Chair of Medicine at Kyoto University.

Dr. Yamada recruited Dr. Kolars to the U-M in 1987. "Tachi was one of my most influential mentors for international activities," noted Dr. Kolars, who has served as the first Senior Associate Dean for Education

and Global Initiatives at the University of Michigan Medical School (UMMS) since 2009.

**CHUNG OWYANG, MD**, succeeded Dr. Yamada as Division Chief in 1990 and continued building international collaborations. Dr. Owyang has helped train a generation of academic gastroenterologists in China and made significant contributions to medical training and the teaching of clinical practice in China, Singapore and Thailand. He played a key role in helping to develop China's first MD/PhD program at Jiao Tong University

in Shanghai and served on its Board of Trustees. He proposed joint research collaborations on gastric cancer and inflammatory bowel disease with Hong Kong University and the Chinese University of Hong Kong that continue today.

In recognition of his contributions to modernizing the Chinese medical training system, Dr. Owyang was awarded honorary professorships by more than 10 top medical schools in China. He served as Chair of the AGA International Committee for two terms (1995 to 1998, 2003 to 2006). During this time, he initiated the first AGA meeting in Asia to promote cross-cultural interaction. This meeting continues to rotate to a different Asian country every year. As Chair of the AGA China Task Force, Dr. Owyang developed a 10-year blueprint



Joseph Kolars, MD



Tachi Yamada, MD, KBE



Chung Owyang, MD

for AGA initiatives in China. In 2015 Dr. Owyang, together with Dr. Gary Wu, organized the first joint meeting with American and Chinese IBD experts in Beijing. This meeting explored factors contributing to the alarming increase of IBD in Asia (*Gastroenterology*, 2016, in press).

Other Division faculty are involved in many additional international collab-

orations, including through Global REACH, a global UMMS initiative led by Dr. Kolars to develop people and programs that improve health and healthcare through international partnerships.

#### **Amplifying Clinical and Translational Research through Collaboration**

Dr. Kolars co-founded and co-directs the University of Michigan and Peking University Health Science Center **Joint Institute for Clinical and Translational Research** ([puuma.org](http://puuma.org)), launched in 2010. Gastroenterology faculty from both institutions and their affiliated hospitals collaborate on a broad range of important clinical GI research projects.

Joint Institute investigations include the effects of diet on irritable bowel syndrome, the role of the microbiome on dysmotility syndromes and development of biomarkers for the diagnosis and management of hepatoma. Researchers also are jointly comparing and contrasting the natural course of viral hepatitis, which has a higher disease burden in China.

"These joint projects are so successful because they build upon synergies between the two institutions," said Dr. Kolars. "Through the Joint Institute, investigators can leverage shared resources, including funding, patient volumes and increased access to new technologies and therapies. It's a win-win that creates many opportunities for mutual learning and discovery."

Gastroenterology and Hepatology faculty from Peking University and the University of Michigan



#### **Thailand: Training medical students and fellows**

In the early 1990s, Dr. Owyang and Dr. Yamada—then serving as president of the American Gastroenterological Association—organized a joint meeting

with the Gastroenterological Association of Thailand (GAT). At the time, Pinit Kullavanijaya, MBChB, DTM&H, PhD, then-professor of gastroenterology at Chulalongkorn University, was serving as president of the GAT.

Since that meeting, the U-M GI Division has maintained close ties with the Chulalongkorn University GI unit. Second-year fellows from the CU GI unit come to Ann Arbor to train with U-M GI faculty during four-week electives. Other fellows from Thailand can spend between one and three years training in research and conducting clinical observation. Many trainees have gone on to become full professors and now hold leadership positions at universities and hospitals throughout Thailand.

"We've been sending our faculty and fellows to the U-M GI Division for more than two decades now, and it has benefited not only the Chulalongkorn University GI Unit specifically but also the gastroenter-



Dr. Owyang with Thai Ambassador His Excellency Pisan Manawapat and his wife, Wanchana Manawapat

ological field generally in Thailand," said Dr. Kullavanijaya.

In recognition of Dr. Owyang's role helping to develop academic gastroenterologists in Thailand, he was elected an honorary fellow of Thailand's Royal College of Physicians in 2011. In 2015, he was honored by His Excellency Pisan Manawapat, Thai Ambassador Extraordinary and Plenipotentiary to the United States.

**Ethiopia: Strengthening academic medical systems**

Although Ethiopia's population tops 90 million, the country is home to only a small number of gastroenterologists. The U-M GI division is helping to change that by co-developing new medical school

and fellowship training programs so that fellows can gain GI training in their home country.

**HARI CONJEEVARAM, MD, MSc**, director of the U-M GI Fellowship Training Program, and colleagues currently are developing curricula and educational models for Ethiopia.



Hari Conjeevaram, MD, MSc

The team has conducted in-country teaching and brought teachers from Ethiopia to U-M to train in new educational methods and helped them set up a new Fellowship Training Program in Gastroenterology. A novel teleconference program enables fellows and teachers in Ethiopia to participate in the U-M GI division's conferences. In addition, GI fellows will come to U-M and U-M GI fellows will also have the opportunity to rotate in Ethiopia.



Gastroenterology and Hepatology faculty from St. Paul's Hospital Millennium Medicine College Addis Ababa, Ethiopia (top) and faculty from the St. Paul's Hospital and the University of Michigan (bottom).

### India: Developing tertiary clinical delivery programs

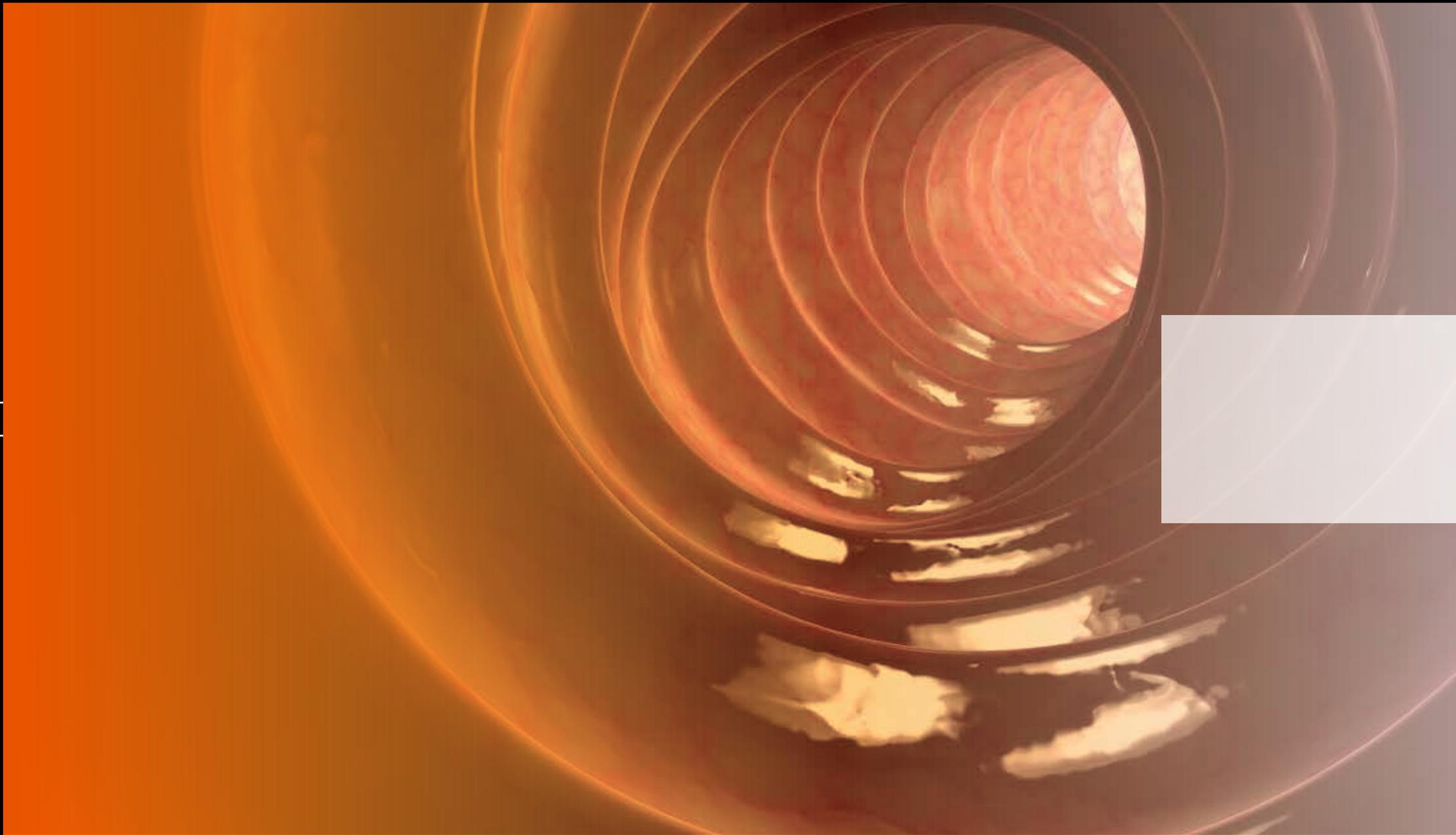
Dr. Conjeevaram and colleagues also have facilitated rotations for U-M GI fellows in India, where he has worked with local healthcare providers to establish a free GI clinic and GI endoscopy unit. In collaboration with the All India Institute of Medical Sciences in New Delhi, he and colleagues from the U-M Department of Internal Medicine are working to develop tertiary-care clinical delivery programs, including programs to address an evolving clinical problem and growing epidemic: fatty liver disease. In 2014, Dr. Conjeevaram took a two-month sabbatical to visit academic institutions in India to educate trainees and explore future collaborative research and learning exchange programs.

Taken together, these and other new programs have amplified the U-M GI division's impact on health and healthcare globally. Dr. Kolars credits the Division with inspiring his own leadership and vision for creating and directing medical training and health system development programs to improve global health.

"When you think about the impact of the Division's global efforts, it's much greater than the impact of specific activities," he said. "A lot of the global health programs I've developed got their footing from my early work in the Division with people like Dr. Owyang and Dr. Yamada. There is a trickle-down effect because of the ways the Division nurtures these connections across borders."



Dr. Conjeevaram with GI and Hepatology fellows from the All India Institute of Medical Sciences, New Delhi, India.



**Recognition + Awards:** HONORING THE LEADERS AND BEST

## Honoring the Leaders and Best

Faculty members of the Division of Gastroenterology and Hepatology have been widely recognized for their service, leadership and notable scientific, clinical and educational achievements, earning many accolades over the years.

### AWARDS

**American Association for the Study of Liver Sciences Distinguished Service Award**  
**ANNA S. LOK** (2011)

**American Digestive Health Foundation**  
**Joseph B. Kirsner Award for Clinical Research in Gastroenterology**  
**CHUNG OWYANG, MD** (1995)  
**Hugh R. Butt Award for Distinguished Achievement in Clinical Research in Hepatology**  
**ANNA S. LOK, MD** (1996)

**American Gastroenterological Association**  
**Julius Friedenwald Medal**  
*The Julius Friedenwald Medal is the highest honor the AGA awards. Established in 1941, it recognizes an individual for lifelong contributions to the field of gastroenterology and service to the association.*  
**CHUNG OWYANG, MD** (2013)  
**TADATAKA (TACHI) YAMADA, MD** (2003)

**William Beaumont Prize**  
*This prize is bestowed upon an individual who has made a unique, outstanding contribution of major importance to the field of gastroenterology.*  
**ANNA S. LOK, MD** (2016)

**Distinguished Clinician Award**  
*The Clinician Award honors practicing physicians who bring scientific knowledge and inquiry to bear on the art of medicine and care of patients.*  
**WILLIAM D. CHEY, MD** (2015)  
**GRACE ELTA, MD** (2013)  
**TIMOTHY T. NOSTRANT, MD** (2012)

**Distinguished Educator Award**  
*Established in 1987, this award recognizes a person's achievements as an outstanding educator over a lifelong career.*  
**JOSEPH KOLARS, MD** (2014)  
**JOHN DEL VALLE, MD** (2012)

**Distinguished Mentor Award**  
*This accolade is given to an individual for achievements as an outstanding mentor over a lifelong career.*  
**M. BISHR OMARY, MD, PhD** (2015)  
**CHUNG OWYANG, MD** (2011)  
**TADATAKA (TACHI) YAMADA, MD** (2010)

**Distinguished Achievement Award in Basic Science**  
*This award honors a senior investigator whose accomplishments in basic research have significantly advanced the science and/or practice of gastroenterology, including hepatology.*  
**JOHN A. WILLIAMS, MD, PhD** (2014)  
**JUANITA L. MERCHANT, MD, PhD** (2017)

**AGA Foundation for Digestive Health and Nutrition Outstanding Women in Science Award**  
*This tribute honors women who have made outstanding contributions to the field of digestive disease science through clinical education, scholarship, research and patient care.*  
**ANNA S. LOK, MD** (2008)  
**JUANITA L. MERCHANT, MD, PhD** (2008)

**American Liver Foundation Distinguished Scientific Achievement Award**  
**ANNA S. LOK, MD** (2008)

**Hepatitis B Foundation Distinguished Scientist Award**  
**ANNA S. LOK, MD** (2008)

## HONOR SOCIETIES—MEMBERSHIPS

### Association of American Physicians Members

JOHN CARETHERS, MD  
ANNA S. LOK, MD  
JUANITA MERCHANT, MD, PhD  
M. BISHR OMARY, MD, PhD  
CHUNG OWYANG, MD

### American Society for Clinical Investigation

JOHN CARETHERS, MD  
JOHN Y. KAO, MD  
JUANITA MERCHANT, MD, PhD  
M. BISHR OMARY, MD, PhD  
CHUNG OWYANG, MD  
ELIZABETH SPELIOTES, MD, PhD, MPH  
ANDREA TODISCO, MD  
THOMAS WANG, MD, PhD  
JOHN WILLIAMS, MD, PhD

## National Academy of Medicine

JOHN CARETHERS, MD  
JUANITA MERCHANT, MD, PhD

## LEADERSHIP

### American Association for the Study of Liver Sciences

ANNA S. LOK, MD  
President (2017)

### American Gastroenterological Association

TADATAKA YAMADA, MD  
President (1996)  
JOHN I. ALLEN, MD  
President (2015)

### American Society for Gastrointestinal Endoscopy (ASGE)

GRACE ELTA, MD  
President (2007)

## American Neurogastroenterology and Motility Society (ANMS)

CHUNG OWYANG, MD  
President (2000–2004)  
JOHN W. WILEY, MD  
President (2014–2016)

## DEPARTMENT OF INTERNAL MEDICINE AWARDS

### Clinical Excellence Society

WILLIAM HASLER, MD (2016)  
PETER HIGGINS, MD, PhD, MSc (2016)  
JOHN DEL VALLE, MD (2015)  
ROBERT FONTANA, MD (2015)  
WILLIAM D. CHEY, MD (2014)  
ERIK-JAN WAMSTEKER, MD (2014)  
GRACE ELTA, MD (2013)  
ANNA S. LOK, MD (2013)  
TIMOTHY T. NOSTRANT, MD (2013)

### Paul de Kruif Lifetime Achievement Award

CHUNG OWYANG, MD (2016)  
KEITH S. HENLEY, MD (2009)

## Editorships

**M. BISHR OMARY, MD, PhD**, Chair of the Department of Molecular and Integrative Physiology and the H. Marvin Pollard Professor of Gastroenterology, served as Editor-in-Chief for *Gastroenterology* from 2011 to 2016. Under his capable leadership, the Impact Factor moved from 11.7 in 2011 to 18.2 in 2016. Many U-M GI faculty, together with faculty from Pathology, Physiology and Surgery, served on the board of editors including Senior Associate Editors **DRS. JOHN CARETHERS** and **CHUNG OWYANG**, and Associate Editors **DRS. WILLIAM HASLER, MALCOLM LOW, ASMA NUSRAT, LINDA SAMUELSON, DIANE SIMEONE** and **JOHN WILLIAMS**. In addition, **JOHN DEL VALLE, GRACE ELTA, ROBERT FONTANA, JOHN**

**KAO, RICHARD MOSELY, JOEL RUBENSTEIN, PHILIP SCHOENFELD, THOMAS WANG** and **JOHN KAO** (Gastroenterology), **JULIE DOUGLAS** (Human Genetics) and **CATHIE SPINO** (Biostatistics) also played key roles as special section editors.

*Gastroenterology* has continued to be the premier journal in the field of digestive health and disease, delivering up-to-date and authoritative coverage of basic and clinical gastroenterology and hepatology. It was a huge honor and a pleasure for the GI division at Michigan to be the home for the top journal in our field.

**WILLIAM D. CHEY, MD**, served as co-Editor-in-Chief of the *American Journal of Gastroenterology* (AJG)

from 2010 to 2015. The Red Journal has an Impact Factor of 10.383 and is the leading clinical journal covering gastroenterology and hepatology. The AJG provides practical and professional support for clinicians dealing with the gastroenterological disorders seen most often in patients. Many of the important guidelines for our practice are published in the journal. GI faculty who served as associate editors include **DRS. HARI CONJEEVARAM, PETER HIGGINS** and **JAMES SCHEIMAN**.

Dr. Chey was the founding co-Editor-in-Chief of *Clinical and Translational Gastroenterology* (CTG), a peer-reviewed open-access online journal dedicated to innovative clinical work in the field of gastroenterology and hepatology. CTG was created to fill

an unmet need for clinicians and scientists by welcoming novel case series and cohort studies, early-phase clinical trials and translational research with clear applications to human physiology or disease. In 2016, CTG achieved an impact factor of 3.472.

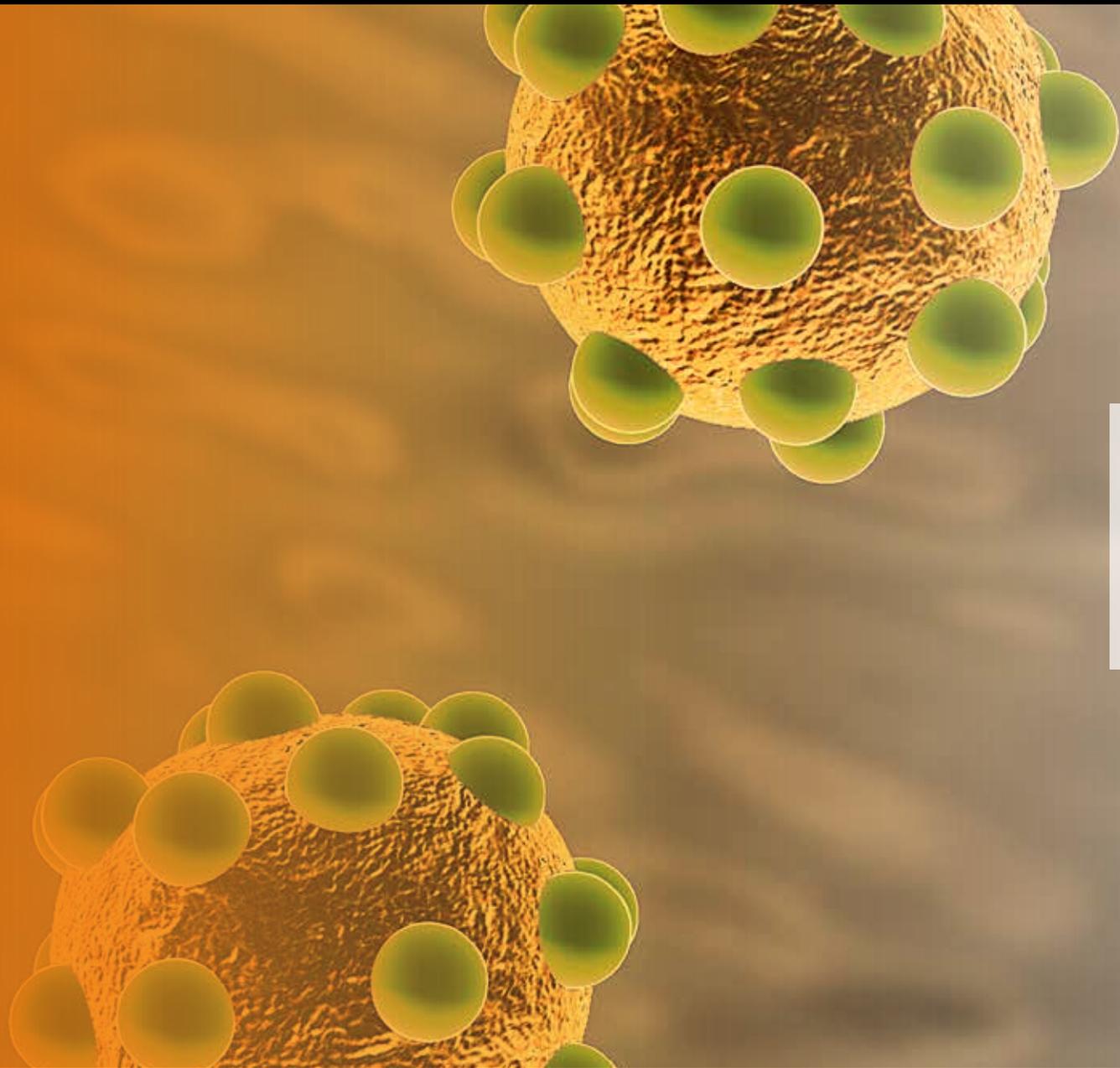


M. Bishr Omary, MD, PhD



William D. Chey, MD





## **Friends + Donors**

## Making a Difference for Others:

NEW GI INNOVATION FUND SUPPORTS ADVANCES IN MEDICINE

In 2013, Mary Petrovich turned 50. She competed in her second U.S. Women's Amateur (golf) Championship, where she made match play and finished in the top 25. A few days after the event, she had her first screening colonoscopy.

But during the procedure Mary's colon was perforated. Her fast-paced life as private equity entrepreneur, mother to two teenagers and nationally competitive golfer was upended, and she underwent several surgeries over the

next six months to try to resolve complications.

A University of Michigan engineering alumna with an MBA from Harvard, Mary analyzed her experience.

"Being an engineer, I began thinking through the failure modes, what happened to me and how it could have been avoided."

She also asked herself two questions that will undoubtedly have a tremendous impact on the lives of others: "What can I do now to make sure this happens to no one else, and what can I do to take this misfortune and turn it into opportunity?"

Mary's answer was to find a way to advance promising innovations in medicine, and she established the Gastrointestinal Innovation Fund at U-M to do just that.

The GI Innovation Fund supports discovery and development of technologies to improve care of patients who suffer from gastrointestinal disease. The fund will support early-stage research, with a particular focus on technologies that could lessen the need for invasive procedures.

Mary was motivated to create the GI Innovation Fund at the U-M because of the "cutting-edge" work she saw

going on within the Division and the U-M Medical School, including many collaborative efforts combining medicine, engineering and other disciplines pursuing biomedical research.

Projects supported by the Fund already are underway, including several related to the use of predictive tools to identify which individuals might benefit the most from colonoscopy and ways to improve procedure-related safety.

In spite of her own difficult experience, Mary sees opportunity. As she told GI division faculty, staff and friends during the 75th Anniversary Symposium, "I'm thrilled to help make a difference with you for others."



Mary Petrovich

## Donor Honor Roll

Gifts from individuals, foundations and corporations enable the Division of Gastroenterology to train the world's best physicians, provide exemplary patient care and to conduct innovative research. This list acknowledges individuals who made outright gifts, new pledges, pledge payments and planned gift including bequests of \$1,000 through November 2016.

### \$1,000,000 and above

Shirley M. McLaughlin Trust  
Crohn's & Colitis Foundation  
of America, Inc.  
Doris Duke Charitable Foundation  
Mr. and Mrs. Charles J. Andrews  
TUKTAWA Foundation

### \$500,000 to \$999,999

American Association for the Study  
of Liver Diseases  
Foundation for Digestive Health  
and Nutrition  
American Digestive Health  
Foundation  
Mr. and Mrs. Scott W. Petrovich

### \$100,000 to \$499,999

American Gastroenterological  
Association Foundation  
American Diabetes Association, Inc.  
American Gastroenterological  
Association  
GlaxoSmithKline  
Dr. Chung Owyang and  
Mrs. Jeannette Owyang  
The Damon Runyon Cancer Research  
Foundation  
Ms. Carol L. Osmer  
The American Society for  
Gastrointestinal Endoscopy  
Dr. Keith Henley\* and  
Mrs. Marcelle Henley\*

Mr. and Mrs. Roy H. Henley  
Johnson & Johnson  
Glaxo Wellcome, Inc.  
Novartis  
American Association for  
Cancer Research, Inc.  
Mr. Edward Ravitz\*  
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Thomas H. C. Cheung Foundation  
Limited  
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Dr. Timothy T. Nostrant \* and  
Mrs. Cynthia A. Nostrant  
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Robert Wood Johnson Foundation  
Eli and Edythe L. Broad Foundation  
Dr. Kamal Gupta and Dr. Nisha Gupta  
Novartis Pharmaceuticals Corporation  
Juvenile Diabetes Research Foundation  
International  
Anonymous Donor  
Novartis US Foundation  
Sandoz Research Institute  
Mr. Kevin Cheng Zou  
The National Pancreas Foundation  
March of Dimes Birth Defects  
Foundation Metropolitan Detroit  
Division  
Janssen Pharmaceuticals, Inc.  
Dr. Henry Van Dyke and  
Dr. Rebecca W. VanDyke  
Rockefeller Brothers Fund  
SmithKline Beecham Corporation  
The Ravitz Foundation

**\$100,000 to \$499,999**

Sonoz Forschungsinstiut  
 Mrs. C.K. Hui  
 Ms. Pearl Hui  
 Mr. and Mrs. William Hui  
 Mr. and Mrs. David Kwan  
 Taisho Pharmaceutical Co., Ltd.  
 The Hartwell Foundation

**\$50,000 to \$99,999**

Cystic Fibrosis Foundation National  
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 Dr. Anna S. Lok  
 Mr. and Mrs. Theodore J. Green  
 Greenview Foundation Hepatitis C  
 Research Fund  
 Ms. Lorilee Babb\*  
 Integrated Therapeutics  
 Elizabeth E. Kennedy Fund  
 Mr. Donald Osmer  
 Procter & Gamble Company

Eli Lilly and Company  
 The American College of  
 Gastroenterology  
 The Greenwall Foundation  
 Blue Cross Blue Shield of Michigan  
 Rome Foundation for Disorders of  
 Gastrointestinal Function  
 Solvay Pharmaceuticals  
 Galecto Biotech  
 Janssen Pharmaceutical Research  
 Foundation  
 P&G Company  
 Searle Research & Development  
 Covance  
 American Society of Transplantation  
 Global Probiotics Council

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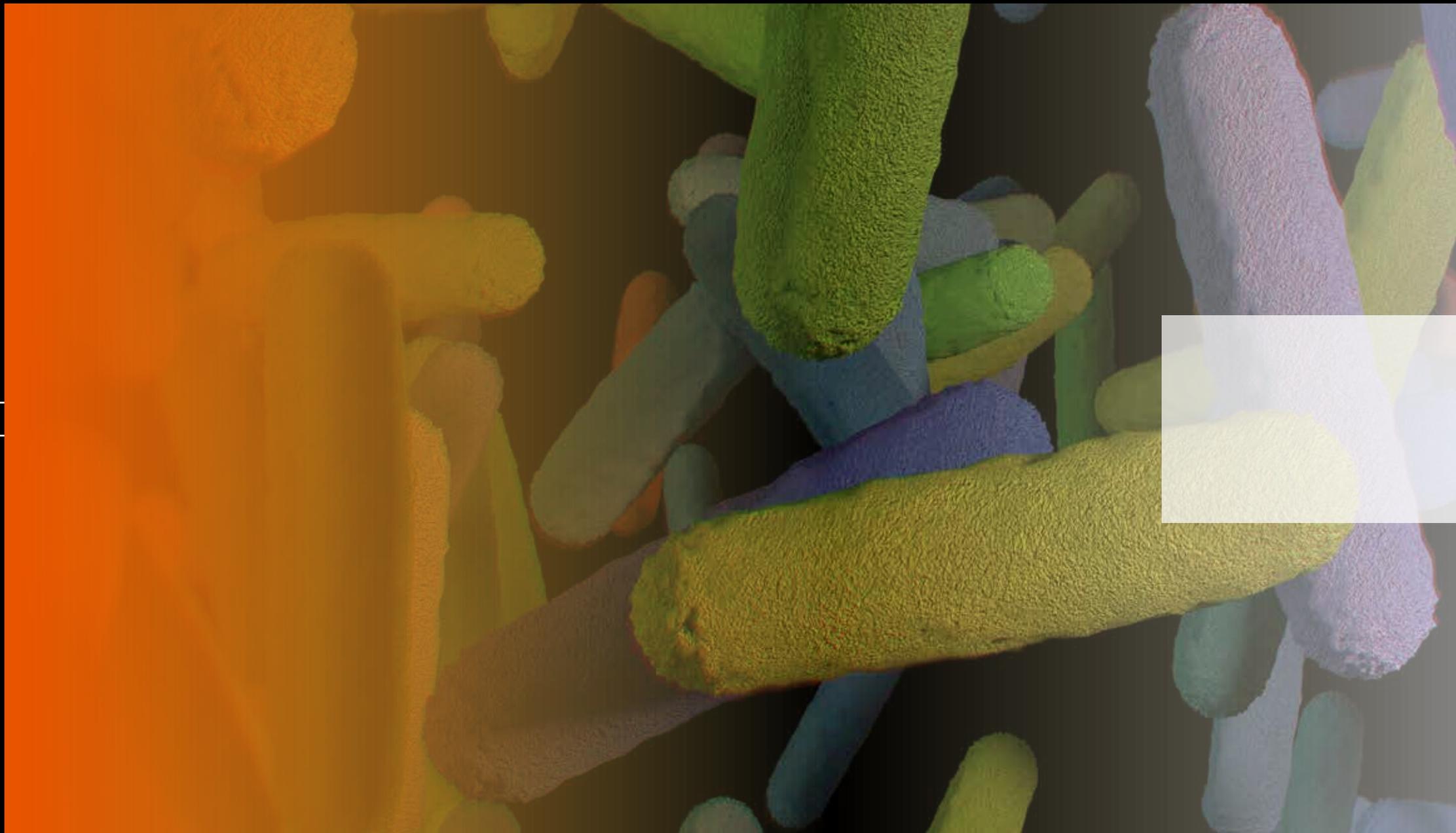
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# **Poised for Growth**



RESEARCH PROGRAMS

- Stem Cell Biology
- Gut Microbiome
- Epigenetics
- Genomic Medicine

**The Future of Gastroenterology:**  
 THE CENTER FOR DIGESTIVE AND LIVER HEALTH

The practice of gastroenterology and hepatology has changed dramatically since the founding of the Division 75 years ago. Advances in molecular biology, genetics, biochemistry, innovative imaging techniques and bioinformatics have contributed to an explosion of new scientific information that has fundamentally changed the way we diagnose, treat and prevent disease.

The Division, with its talented investigators and masterful clinicians, is well prepared to explore unparalleled opportunities and address new challenges to improve our understanding of complex disease processes. As we work to devise new approaches to disease treatment and prevention, the Division remains steadfast in its pursuit of its tripartite missions: research, clinical care and education.

**Research**

Advances in medicine depend on the acquisition of new information through research, and the third millennium ushers in the era of "omics."

Advances in genomics, epigenomics, proteomics, microbiomics, metagenomics and metabolomics have significantly altered our concept of disease pathogenesis and have opened a portal for formulating new treatments for challenging GI disorders.

In the next 10 years the Division will focus on four major themes:

**Stem cell biology** continues to be an area of emphasis of our research. Stem cells play a critical role in maintaining normal tissue function and in the development of cancer and degenerative GI disorders. The program project, "Cellular decisions

on proliferation, differentiation and apoptosis," initiated by **DRS. MERCHANT, SAMUELSON and GUMUCIO** in 2003 paved the way for our stem cell biology research program. The recent establishment of the organoid program by **DR. JASON SPENCE** allows investigators to grow intestine as three-dimensional structures from pluripotent stem cells and provides innovative tools to study stem cell interactions with the environment.

The Division will continue to recruit physician scientists with expertise in stem cell research and expand upon

this program to explore the emerging role of stem cells in the treatment of a variety of GI disorders.

The recently initiated **Gut Microbiome Project**, initiated by **DRS. VINCENT YOUNG, JOHN KAO** and **CHUNG OWYANG**, will continue to expand. Advances in DNA sequencing technology combined with new bio-computational tools enable scientists to describe our microbial environment with greater precision. The genomic revolution offers an exceptional opportunity to identify the molecular mechanisms governing commensal host-bacterial relationships. This knowledge helps us understand how such interactions contribute to normal physiology and provides the foundation necessary to formulate normal therapeutic strategies in inflammatory bowel

disease (IBD), irritable bowel syndrome (IBS) and metabolic disorders.

The Division is fully committed to expanding the **Epigenetics Program**, recently initiated by **DR. JOHN WILEY**. Basic and clinical studies indicate that alteration in gene function can occur without changes in DNA sequence. This may occur through DNA methylation, histone modification and chromatin remodeling. Epigenetic alterations are associated with a number of chronic disorders including GI cancers, aging, degenerative diseases, chronic pain syndromes and eating disorders.

The groundbreaking work of Dr. Wiley on epigenetics pathways in stress and abdominal pain and **DR. JOHN KAO'S** research on epigenetic alteration of the gut immune system in

gut dysbiosis are beginning to lay the foundation for forming an Epigenetic Research Program in the GI Division.

The **Genomic Medicine Program** allows physicians to develop targeted approaches to the treatment of GI disorders. The completion of the Human Genome Project provides new opportunities to pursue personalized medicine. Gene expression profiles may be used to guide therapy and inform prognosis for a variety of disorders. In fact, the use of genotyping may provide a new way to assess the risk of certain diseases as well as variation in response to different drugs. Research from **DR. ELIZABETH SPELIOTES** sheds light on the role of certain genes in the causality of common conditions such as obesity and non-alcoholic fatty liver disease (NA-

FLD). This information also provides novel targets for intervention and prevention. Under the leadership of Dr. Speliotes, the Genomic Medicine Program will continue to grow.

#### **Clinical Care**

We take pride in our multidisciplinary approach to care for patients with complex GI issues. This includes our **IBD, IBS and pancreatic and biliary disorders clinical programs**. In the coming year, we plan to use a similar blueprint to establish a **non-alcoholic steatohepatitis (NASH)** Multidisciplinary Program at the University of Michigan. NASH is the most common liver disease in the United States and is predicted to become an increasingly important cause of liver-related

### **PROPOSED CENTER FOR DIGESTIVE AND LIVER HEALTH**

- Improve the patient experience
- Allow for growth of Digestive and Liver Health Programs
- Increase the presence of U-M within the local and national communities
- Support GI education and research

morbidity and mortality. Metabolic changes associated with obesity are the predominant drivers of NASH. Although pharmacotherapy for NASH is an active area of translational research and clinical trials, there are currently no FDA-approved therapies. However, clinical studies suggest modest weight loss may result in histological improvement in NASH. Hence, we propose the development of a multi-interventional weight loss program for NASH treatment. This will involve lifestyle modification, nutrition education, fecal transplant and bariatric endoscopic and surgical intervention.

The increasingly popular utilization of telemedicine heralds great promise in the field of gastroenterology, especially in treating patients with

chronic GI disorders. The Division will focus on the development of a **GI Telemedicine Program**. This will further contribute to improved accessibility and lessened chronic burden for patients who have to travel long distances to our Medical Center for their clinical care. At the same time, the Telemedicine Program will facilitate efficient resource utilization for the Medical Center while enhancing continuation care and followup, leading to improved clinical outcomes.

To enhance our clinical growth and improve the patient experience and clinical outcomes, the Division proposes the development of a **Center for Digestive and Liver Health (CDLH)**. The Center, conceptually similar to the U-M Cardiovascular Center, would provide coordinated,

multidisciplinary care in a state-of-the-art environment. The proposed facility would comprise 200,000 sq. ft. and include a 12- to 14-room endoscopy suite, 40 exam rooms, dry lab space, a call center, conference rooms, auditorium, pharmacy and a test kitchen.

With the CDLH, the Division will be able to provide clinical services in one location, with multiple specialties under one roof, to foster collaboration and communication. By adding the space, the Division will be able to expand clinical and endoscopic activity, developing an innovative food-centric program and telemedicine infrastructure. The proposed CDLH will help to facilitate clinical trials and offer personalized medicine and health service research.

### Education

Training the next generation of gastroenterology leaders is a major mission of the Division. The University of Michigan is recognized both for its clinical training as well as for its top-ranked training in basic science and outcomes and health service research. The rapid advances in molecular biology, biochemistry and genomics has significantly altered the way we practice medicine. As a result, the Division is revamping its core curriculum to include findings garnered from this explosion of scientific information so that our trainees become familiar with the fields of genomics, epigenomics, proteomics and bioinformatics in order to integrate scientific advances into their clinical practice.

The Division takes an individualized training approach to bring out the best in each trainee. We will continue to diversify our training to include novel programs, including the National Clinician Scholar Program and Graduate Medical Education Scholar Program to train clinical educators and the Innovation and Entrepreneurship Program to train physicians interested in translating scientific findings into clinical products.

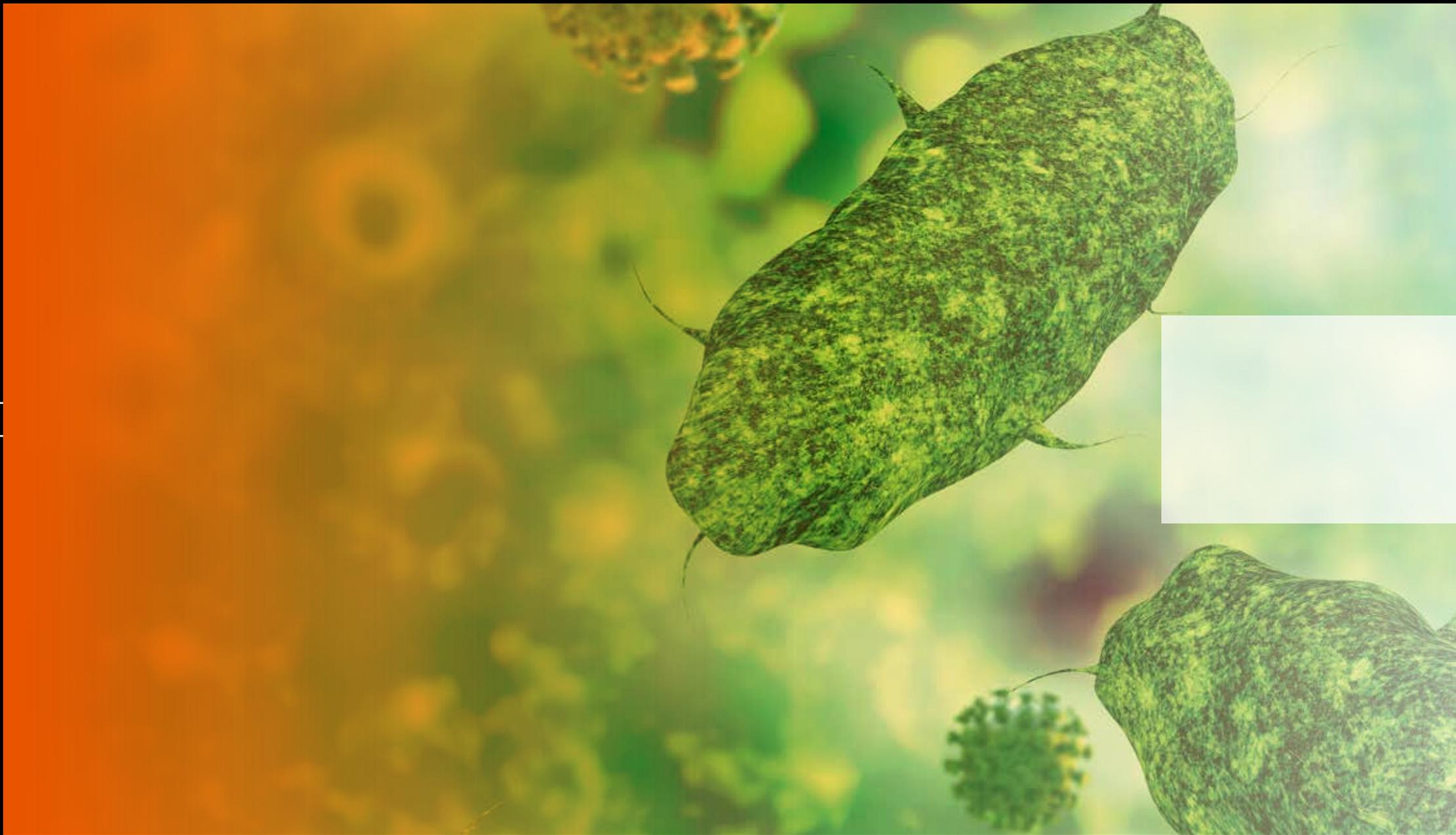
Under the leadership of **DR. JOHN ALLEN**, the Division is developing a business and leadership training program, which will allow trainees to obtain a master's degree in business administration. The new program is tentatively named, **"Life, Leadership, and Legacy"** and will educate interested fellows

in career planning, financial and practice management, organizational leadership and healthcare policy. It will draw upon the University's wealth of resources and expertise in business administration, healthcare management, public policy and clinical intervention.

Since its founding 75 years ago, the Division has become one of the nation's preeminent centers for the prevention, diagnosis and treatment of disorders of the digestive tract and liver. We are proud of our past achievement and optimistic about shaping the future. With our commitment to scientific discovery and the clinical excellence of our faculty and trainees, we will remain "always healing, forever valiant."

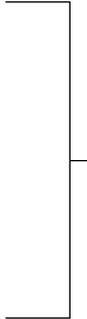
#### GI FELLOWSHIP PROGRAM

- **Physician Scientist Training Program**
- **Outcome Research Training Program**
- **National Clinician Scholar Program**
- **Graduate Medical Education Scholar Program**
- **Innovation and Entrepreneurship Program**





**Celebrate!**



## GI and Hepatology at the University of Michigan:

PAST, PRESENT AND FUTURE OF INNOVATION, CLINICAL PRACTICE AND LEADERSHIP



Chung Owyang, MD

In September 2016, the Division of Gastroenterology and Hepatology celebrated the 75th anniversary of the founding of the Division. As part of that celebration the Division held a two-day symposium, **"GI and Hepatology at the University of Michigan: Past, Present and Future of Innovation, Clinical Practice and Leadership."**

The Thursday program, moderated by Drs. Chung Owyang and William Chey, included Dr. John Carethers, followed by leaders in gastroenterology and hepatology from across the nation including Drs. Tachi Yamada, Rick Boland and David Lieberman. Distinguished alumni speakers included Drs. Ezra Burstein, Joseph Elmunzer, Michael Kochman, Uri Ladabaum, John Inadomi and Michael Lucey.

The Friday program, moderated by Dr. Juanita Merchant, showcased the achievements of some of our own U-M faculty, including Drs. Anna Lok, Liz Speliotes, John Allen, John Wiley, Peter Higgins, William Chey, Hari Conjeevaram, Thomas Wang, Jason Spence and Nobu Kamada. Mary Petrovich, a philanthropist and friend to the Division, was also on hand to give her personal reflection on patient care and the future of innovation.

On Friday, Medicine Grand Rounds was presented by a special guest, Dr. Daniel K. Podolsky, President of UT Southwestern Medical Center.



**JOHN I. ALLEN MD, MBA, AGAF**

*Professor of Internal Medicine;  
Professor of Gastroenterology  
Division of Gastroenterology and  
Hepatology  
University of Michigan Medical School*

### What's Next for GI—The Red Queen

Current changes in healthcare delivery and payment will test the strength and creativity of health systems including the University of Michigan. We will feel like the Red Queen from *Alice in Wonderland*, who said we must run as fast as we can to stay in one place—twice as fast to move ahead. Health systems that can coordinate care and learn how to care for high-cost patients in the most efficient manner with the highest quality will emerge as strong leaders. That is our intention here.



**WILLIAM CHEY, MD, FACG, AGAF**  
*Timothy Nostrant Collegiate Professor of GI & Nutrition Sciences; President, Clinical Excellence Society; Director, GI Physiology Lab; Director, Digestive Disorders Nutrition & Lifestyle Program; Medical Director, Michigan Bowel Control Program  
University of Michigan Medical School*

### **The University of Michigan Experience with the Low-FODMAP diet**

It is increasingly clear that nutrition plays a pivotal role in the pathogenesis and treatment of many gastrointestinal disorders. At present, the best evidence supporting dietary therapies exists for the irritable bowel syndrome (IBS). Food can trigger IBS symptoms through direct and indirect effects on motility, visceral sensation, brain-gut interactions, gut microbiome, intestinal permeability and gut immune function. Recent randomized, controlled trials, including data generated at U-M's Digestive Disorders Nutrition & Lifestyle Program (DDNLP), support the efficacy of the low-FODMAP diet and gluten-free diet in IBS patients. In

addition to building a robust clinical infrastructure to provide holistic, integrated care to patients with IBS and other GI disorders, DDNLP will conduct cutting-edge translational and clinical research and create unparalleled training opportunities for physicians and allied health providers.



**HARI CONJEEVARAM, MD, MSc**  
*Professor of Medicine  
Program Director, Gastroenterology Fellowship Training  
University of Michigan Medical School*

### **Fellowship Program**

The GI fellowship program at the University of Michigan has enjoyed a rich history and the program today is quite robust. The program highlights include many educational, research and innovative projects, with new programs in development, to train the next generation of gastroenterologists.



**PETER D. R. HIGGINS, MD, PhD, MSc**  
*Associate Professor of Medicine  
University of Michigan Medical School*

**Machine Learning in Gastroenterology and Hepatology**

Machine learning can identify patterns in laboratory data that can predict disease progression and response to medications. We have shown that this is valuable for hepatitis C, prediction of success with thiopurines in IBD and response to vedolizumab in ulcerative colitis.



**NOBU KAMADA, PhD**  
*Assistant Professor, Gastroenterology  
University of Michigan Medical School*

**A Battle Within: Competition Between Good and Bad Bacteria in the Gut**

We found that inflammation-induced metabolic reprogramming in *E. coli* promotes the selective growth of pathogenic *E. coli* at the expense of its commensal counterparts. Depriving pathogenic bacteria of preferred nutrients suppresses their ability to bloom in the gut.



**ANNA S.F. LOK, MD, FRCP**  
*Assistant Dean for Clinical Research;  
Alice Lohrman Andrews Research  
Professor of Hepatology; Professor  
of Internal Medicine and Director of  
Clinical Hepatology  
University of Michigan Medical School*

### **From Non-A, Non-B Hepatitis, to Hepatitis C Cure, to Global Elimination of Hepatitis C**

There has been miraculous progress from non-A, non-B hepatitis—a term coined for hepatitis C in the 1970s—to discovery of hepatitis C virus in 1989 and the development of blood tests to diagnose and screen blood products for hepatitis C in 1991, to the approval of combinations of oral antiviral agents that can achieve virologic cure in more than 95 percent of patients in 2014. The remarkable progress in hepatitis C has not been seen in any other field of medicine and has already translated to a decrease in number of patients listed for liver transplantation.



**JASON SPENCE, PhD**  
*Associate Professor of Internal Medicine, Gastroenterology; Associate Professor of Cell and Developmental Biology  
University of Michigan Medical School*

### **Modeling Human Development Using Insights from Organoids and Embryos**

Dr. Spence presented work from his laboratory highlighting how they are implementing 3-dimensional human pluripotent stem cell derived intestinal organoids to investigate human intestine development, and to understand how microbes (bacteria) that colonize the neonatal gut interact with the intestinal epithelium, leading to enhanced intestinal maturation and function, or to epithelial damage and disease.



**ELIZABETH SPELIOTES, MD, PhD, MPH**  
*Associate Professor  
University of Michigan Medical School*

Genomics has identified that susceptibility to becoming obese or developing NAFLD lies in nervous system genes/pathways and liver lipid/glucose metabolism respectively.

Even though obesity and NAFLD are epidemiologically highly related to each other, genetics can point to distinct etiologies that can be specifically targeted to aid in precision therapies for these conditions.



**THOMAS WANG, MD**  
*H. Marvin Pollard Collegiate Professor of Endoscopy Research; Professor, Internal Medicine, Biomedical Engineering, Mechanical Engineering University of Michigan Medical School*

**Imaging the Serrated Pathway for Colorectal Cancer**

A targeted imaging method for early detection and prevention of colorectal cancer was presented using a fluorescence labeled peptide that binds specifically to overexpressed cell surface targets in sessile serrated adenomas.



**JOHN W. WILEY, MD**  
*Professor of Internal Medicine; Director, Michigan Clinical Research Unit*

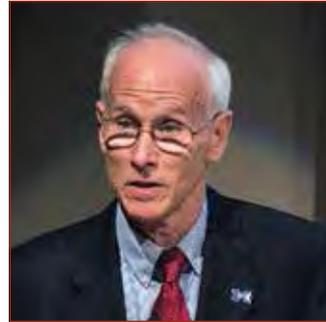
Chronic stress is associated with enhanced abdominal pain, particularly in patients with functional GI disorders such as irritable bowel syndrome. Recent evidence suggests

that altered gene expression involving epigenetic regulatory pathways may play an important role to explain why these patients experience enhanced abdominal pain.



**C. RICHARD BOLAND, MD, AGAF**  
*Emeritus  
Professor of Medicine  
Baylor University Medical Center  
(BUMC), Dallas, Texas*

**An Overview of the Discovery of  
the Familial Colorectal Cancer  
Genes**



**DAVID A. LIEBERMAN, MD**  
*Professor of Medicine  
Chief, Division of Gastroenterology/  
Hepatology  
Oregon Health & Science University*

**Settled and Unsettled Issues in  
2016**



**EZRA BURSTEIN, MD, PhD**  
*Associate Professor of Internal  
Medicine and Molecular Biology  
Chief, Division of Gastroenterology /  
Hepatology  
UT Southwestern Medical Center*

**Understanding Pathologic  
Inflammation and IBD in the  
Genomic Era**



**BADIH JOSEPH ELMUNZER MD,  
MSc**  
*Associate Professor  
Peter B. Cotton Chair for Endoscopic  
Innovation  
Department of Internal Medicine  
Medical University of South Carolina*

**Clinical Trials in GI Endoscopy**



**STEVEN CARPENTER MD**  
*Academic Chair  
Department of Internal Medicine  
Memorial University Medical Center,  
Savannah, Georgia*

**Managing Outpatient Clinical  
Issues In GI: An Evidence-Based  
Update**



**MICHAEL LEE KOCHMAN, MD**  
*Wilmott Family Professor of Medicine and Professor of Medicine in Surgery  
Director, Center for Endoscopic Innovation, Research, and Training  
Perelman School of Medicine  
University of Pennsylvania*

**Incorporation of Innovation into Gastroenterology: Moving the Boundaries**



**URI LADABAUM, MD**  
*Professor of Medicine, Senior Vice Chief  
Director, Gastrointestinal Cancer Prevention Program  
Division of Gastroenterology and Hepatology  
Stanford University School of Medicine*

**Risk Stratification in Colon Cancer Screening**



**JOHN M. INADOMI, MD**  
*Cyrus E. Rubin Endowed Chair in Medicine  
Professor of Medicine and Head  
Division of Gastroenterology  
University of Washington*

**Barrett's Esophagus**



**MICHAEL R. LUCEY, MD**  
*Chief, Gastroenterology and Hepatology  
Professor of Internal Medicine  
University of Wisconsin School of Medicine*

**Liver Transplantation and Alcohol: an Uneasy Mix**



**DANIEL K. PODOLSKY, MD**  
*President, UT Southwestern Medical Center*

**Tale of the Vasa and the Future of Academic Medical Centers**







## Dinner

As part of the Division's 75th anniversary celebration, a celebratory dinner was held at the U-M's Museum of Art. The beautiful surroundings, amazing food and captivating speakers made it a very special event.





## Let's Go Blue!

It wasn't all lectures and grand rounds for 125 Symposium attendees. On Saturday, attendees could be found at a tailgate before proceeding on to the Big House, where they watched the Wolverines beat Penn State 49-10.





## Colleagues, Alumni and Friends,

It is my great honor and pleasure to congratulate the Division of Gastroenterology and Hepatology on its 75th anniversary.

The Division is one of the largest and most innovative academic gastroenterology and hepatology practices in the United States, successfully delivering outstanding care to patients across Michigan and beyond. In 2016, the faculty conducted more than 41,000 outpatient visits and performed over 30,000 endoscopies. Research accomplishments continue to gain momentum, with \$15 million in research funding in 2015.

Together, the Division's scientists and clinicians are advancing discovery in the broad area of gastrointestinal diseases through major fundamental and clinical research initiatives. Since 2009, more than 31,000 patients have partic-

ipated in 415 clinical studies, in many cases gaining access to novel therapies available at few other institutions.

These innovations and breakthroughs have made it possible for our patients to receive the very latest, highest-quality care.

The Division's success is built upon the foundation laid and sustained by visionary leaders: Drs. Pollard, Henley, Nostrant, Yamada and, since 1990, Owyang. Along with leading departmental growth, Dr. Owyang has further built this vision over the past 26 years by creating an environment to ensure ongoing breakthroughs in the diagnosis, management and treatment of the most challenging

disorders in the field. In areas such as bioinformatics, personalized medicine, epigenetics and multidisciplinary care, cross-functional collaborations are rapidly changing what will be possible in the future of gastrointestinal care.

The Division's past, present and future have also been supported by the incredible generosity of many donors. Their gifts have supported professorships and investigational efforts that enable our faculty to carry out our research, clinical care and educational missions.

A core part of our mission across the University of Michigan Medical School and Health System has been to train and prepare the next generation of

physicians and scientists. Over the past 50 years, the Division of Gastroenterology and Hepatology has trained more than 400 gastroenterologists and hepatologists to be leaders in the field worldwide.

To the Division's dedicated faculty, staff and leadership, and to Drs. Owyang and Carethers, the University of Michigan Medical School congratulates you on 75 years of success and thanks you for your commitment to discovery and healing.



**MARSCHALL S. RUNGE, MD, PhD**

*Executive Vice President for Medical Affairs*

*Dean, University of Michigan Medical School*

## Acknowledgements

I would like to express my sincere gratitude to every person whose hard work and dedication to the Division has made our 75 year journey truly remarkable. Our Division today is fortunate to be enriched not only by our faculty, fellows and investigators, but by over 150 talented staff. Every individual's contribution is invaluable and very much appreciated.

Following the 75 th Anniversary Celebration I received many heartfelt messages from guests letting me know how much they enjoyed themselves at the events. I would like to thank the following individuals for their tireless efforts to ensure the celebration was an overwhelming success.

**Jeff Holden, MBA**, Division Administrator, Division of Gastroenterology and Hepatology

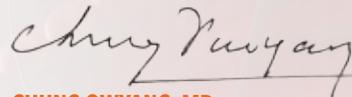
**Theresa Nester**, Administrative Specialist, Division of Gastroenterology and Hepatology

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**Bill Burgard**, Lecturer II, Stamps School of Art and Design

**Hilary Robinson**, Associate Director, Michigan Creative, and the Michigan Creative team including, **Martin Soave** and **Ruth Gretzinger**, and also **Kim Roth**, from Outword Communications

Sincerely,



**CHUNG OWYANG, MD**,  
Chief, Division of Gastroenterology  
and Hepatology



Liver

Stomach

Small Int

Large Intestine