We are thrilled to share with you this report showcasing some of the highlights of our work in Gastroenterology and GI Surgery over the past year.

We are proud to collaborate with our colleagues nationwide to help lead the advancement of scientific knowledge and, ultimately, the provision of state-of-the-art clinical care for patients with complex gastrointestinal diseases. Our faculty are pioneering the use of robotic endoscopy and artificial intelligence technologies to detect and treat gastrointestinal lesions. Our researchers are gaining new insights into the role of the gut microbiome in pancreatic cancer. And our IBD Center is conducting cutting-edge research; providing a precision-medicine approach to care; and performing the most complex IBD surgeries.

Please read on to learn more about the exciting advances that are improving care for our patients and the patients of tomorrow.
CLINICAL TRIALS PROVIDE ACCESS TO CUTTING-EDGE THERAPIES

At the IBD Center, led by Feza Remzi, MD, professor of surgery and center director, and David P. Hudesman, MD, associate professor of medicine and center co-director, patients have access to a full spectrum of advanced diagnostics, treatments, and procedures. For patients with Crohn's disease (CD) or ulcerative colitis (UC) who may be in need of new options for inducing or maintaining remission, the center's participation in clinical trials is an important component in making investigational treatments and approaches available.

Dr. Hudesman is leading an investigator-initiated study that seeks to individualize UC treatment through the use of patients' cellular and molecular profiles obtained from blood and stool samples. These samples are used to identify characteristics in patients with UC that may predict response to the drug tofacitinib. “Over the past few years, new drugs for managing UC have come to market with novel mechanisms of action,” says Dr. Hudesman. “It is important that we study how to incorporate these new medical options into clinical practice and find the right medication for the right patient.”

There are also opportunities for participation in ongoing research through other clinical trials and multicenter collaborative registries, such as the VICTORY Consortium, which uses patient data to establish the real-world efficacy and safety of current immunosuppressant and biologic agents. In general, active research programs such as these result in the rapid translation of findings in the lab to new treatment options in clinical care.

RESEARCH SUGGESTS POTENTIAL ENVIRONMENTAL TRIGGER FOR IBD FLARES

Observational studies have demonstrated a correlation between dysbiosis in the gut microbiome and IBD; however, the mechanisms of dysbiosis remain unknown. In a recently published cross-sectional analysis of more than 9,000 patients experiencing a diarrheal illness, Jordan E. Axelrad, MD, MPH, instructor of medicine and a translational researcher with the IBD Center, and colleagues used multiplex stool PCR testing to examine...

It is important that we study how to incorporate new medical options into clinical practice and find the right medication for the right patient.”

—David P. Hudesman, MD
Under the guidance of Feza Remzi, MD, professor of surgery and director of the Inflammatory Bowel Disease (IBD) Center, surgeons at the center perform a high volume of surgical procedures. “Experience guides innovation and outcomes,” notes Dr. Remzi, “and complex operations should be performed by surgeons who do them every day.”

In a recent case, the multidisciplinary team was well-equipped to diagnose and treat a patient with complicated Crohn’s disease (CD) who presented to NYU Langone with a reported history of irritable bowel syndrome (IBS). Suspecting that IBS was a misdiagnosis, Mark B. Pochapin, MD, the Sholtz/Leeds Professor of Gastroenterology, director of the Division of Gastroenterology & Hepatology, and vice chair of Clinical Affairs in the Department of Medicine, immediately referred the patient to David P. Hudesman, associate professor of medicine and co-director of the IBD Center. MR enterography showed complicated Crohn’s ileitis with a phlegmon. Dr. Hudesman consulted Dr. Remzi, and together the two physicians discussed with the patient that she would likely need surgery given her penetrating CD, but that medication could be tried first. She was started on infliximab, which led to an initial improvement in her symptoms but then her abdominal pain recurred and the phlegmon progressed. Dr. Remzi then performed a laparoscopic small bowel resection and found a large phlegmon, a small mesenteric abscess, and a fistula from the ileum to the transverse colon. Tissue friability and perforation, with extensive adhesions and fibrotic scar tissue, offered additional challenges. Ultimately, Dr. Remzi and the team successfully resected the fistula with ileocolic resection and drainage of the mesenteric abscess. Followed by primary end-to-side anastomosis without the need for ileostomy. The patient recovered without complications. Because the patient was at high risk of Crohn’s recurrence, she was continued on infliximab postoperatively. Repeat colonoscopy at one year did not show any evidence of recurrence of disease. Recently married, the patient has been referred to the IBD Center’s preconception counseling program to discuss pregnancy and IBD and the importance of remaining on medication throughout pregnancy.

Experience guides innovation and outcomes, and complex operations should be performed by surgeons who do them every day.” —Feza Remzi, MD

**Complex Case: Successful Laparoscopic Ileocele Resection in Complicated Crohn's Disease with Ileotransverse Fistula**

**PREOPERATIVE MRI IMAGES GUIDE SURGICAL PLANNING**

1. Coronal HASTE images through the abdomen and pelvis show an inflammatory mass in the right lower quadrant (arrow) with fistulous communication to the inflamed transverse colon (arrowheads).

2. Axial T1-weighted fat saturated images (GRASP sequence) show an inflammatory mass in the right lower quadrant (arrow) with fistulous communication to the inflamed terminal ileum and transverse colon (arrowheads).
GUT BACTERIA MIGRATE TO THE PANCREAS THROUGH
THE PANCREATIC DUCT

The microbiome in the pancreas increases by more than a thousandfold in patients with pancreatic ductal adenocarcinoma (PDA) and becomes dominated by species that prevent the immune system from attacking tumor cells, according to a murine and human study led by researchers at Perlmutter Cancer Center. Their investigations were published online in March 2018 in Cancer Discovery.

The researchers found that in patients with PDA, pathogenic gut bacteria migrate to the pancreas through the pancreatic duct. Once in the pancreas, this altered microbiome triggers immune cell checkpoints that inhibit the immune system and promote cancer growth, according to the authors. Specifically, the study suggests that the bacteria that are more abundant in pancreatic cancers—including Proteobacteria, Actinobacteria, and Fusobacteria—release lipopolysaccharides and flagellins that shift macrophages into immune suppression.

"While combinations of changes in genes like KRAS cause cells to grow abnormally and form pancreatic tumors, our study shows that bacteria change the immune environment around cancer cells to let them grow faster in some patients than others, despite their having the same genetics," says senior study co-author George Miller, MD, the H. Leon Pachter, MD, Professor of Surgery, professor of cell biology and co-leader of the Tumor Immunology Research Program at Perlmutter Cancer Center.

SYNERGISTIC PROTECTION FROM PDA THROUGH INCREASED T-CELL PRODUCTION

Using a mouse model of PDA, researchers observed that the elimination of bacteria through antibiotics and addition of αPD-1 therapy created a synergistic protection from PDA through increased T-cell production. This spurring of the immune system slowed pancreatic tumor growth and reduced tumor burden by 50 percent (see figure below). "Our study confirmed that, similar to what has been observed in patients with pancreatic cancer, checkpoint inhibition alone did not protect mice. This may be because, in the immunosuppressive environment of the tumor, there are too few immune cells around to be activated," says first co-author Mautin Hundeyin, MD, a postdoctoral fellow in Dr. Miller’s lab.

Gut Microbiome Impacts Tumor Progression in Pancreatic Cancer

Targeting the microbiome protects against oncogenesis, reverses intratumoral immune tolerance, and enables efficacy for checkpoint-based immunotherapy.

Bacteria change the immune environment around cancer cells to let them grow faster in some patients than others, despite their having the same genetics.”

—George Miller, MD

This study was supported by several grants from the National Institutes of Health (CA206505, CA168613, CA155649, DE125992, CA260275, CA275794, N01-DK-25009-95, P50 DK013498), the Department of Defense Peer-Reviewed Medical Research Program, the Lustgarten Foundation, an AACR–PanCan grant, the Pancreatic Association of America, the National Pancreas Foundation, the Crohn’s and Colitis Foundation of America, and the Irene and Bernard Schwartz Fellowship in Gastrointestinal Oncology.
Less-Invasive Lap Band Surgery May Relieve Knee Osteoarthritis Pain

Bariatric surgery reduces obesity and knee osteoarthritis (OA) pain, but some patients improve more than others, according to an NYU Langone Health study. The findings showed that the youngest patients and patients without prior knee injuries experienced the greatest pain relief after one year, regardless of preoperative body mass index (BMI).

Most Relief for Youngest Patients and Patients Without Prior Knee Injuries

For this one-time telephone study, researchers contacted 120 patients who had undergone laparoscopic adjustable gastric banding (LAGB) at NYU Langone between 2002 and 2015 and asked them to rate their knee pain on a 10-point scale before surgery, one year postsurgery, and at the time of the survey. Patients ranged in age from 26 to 69 years, were mostly female and Caucasian, and had an average baseline BMI of 46 kg/m².

Even slight weight loss seems to trigger a decrease in inflammatory markers, which affects how people perceive their knee pain.”

—Christine J. Ren-Fielding, MD
Examining data from a broader cohort of patients having lap band as well as more aggressive weight loss surgeries, the team is investigating the impact of weight loss on underlying biological changes caused by fat tissue and inflammation in the knees. Of particular note are patients who have had the most pain relief one month post-bariatric surgery even though weight loss continued.

In ongoing studies presented at meetings, researchers noted that it appears that levels of the anti-inflammatory marker known as soluble receptor for advanced glycation end products (sRAGE)—which is often low in obese patients—rose during the first month after surgery. Patients had significantly decreased levels of leptin—an inflammatory mediator found in the blood—at one month as well. The investigators are following up on these findings by studying the effects of sleeve gastrectomy on patients with knee osteoarthritis and by examining the microbiome for other inflammatory markers related to knee pain.

“We now have more insight into how bariatric surgery, including LAGB, may lower inflammatory hormones and chemicals that directly affect knee pain and overall joint health,” says Dr. Ren-Fielding. “It appears that even slight weight loss or caloric restriction has an impact on inflammation.”

CALORIC RESTRICTION OR EVEN SLIGHT WEIGHT LOSS CAN AFFECT INFLAMMATION

The findings from these studies have important implications for clinicians treating obese patients, Dr. Ren-Fielding adds. For example, LAGB provides another option for patients with a BMI between 30 and 35 kg/m² and mild to moderate knee pain that does not necessarily require orthopedic surgery. “Our findings show that patients don’t need to lose over 100 pounds or undergo surgeries as severe as stapling or resection to improve their knee pain,” says Dr. Ren-Fielding. “Less invasive LAGB can help people lose enough weight to change the inflammatory state of their body.”

Internationally renowned clinician and researcher Ira M. Jacobson, MD, professor of medicine, joined the Division of Gastroenterology and Hepatology as director of hepatology in 2017. He and his colleagues across the institution continue to build on existing momentum and lead programs aimed at enhancing care for patients with liver disease.
Dr. Jacobson and his colleagues are currently participating in numerous clinical trials in the area of liver disease, including several aimed at finding new treatments for nonalcoholic steatohepatitis (NASH), the most serious form of nonalcoholic fatty liver disease (NAFLD). NASH often goes undiagnosed in its early stages, leaving patients at high risk for cirrhosis, liver failure, and cancer.

The latest experimental treatments target different molecular stages in the disease process, with the goal of slowing or even reversing fibrosis. “NASH is on a trajectory to replace hepatitis C as the leading indicator for liver transplantation, yet there are currently no FDA-approved therapies,” says Dr. Jacobson. “There’s an urgent need to develop new therapies aimed at reversing the progression of fibrosis.”

Investigating New Treatments for Fatty Liver Disease

Included among the clinical trials being conducted at NYU Langone Health are:

- A Phase 3 Double-Bind, Randomized, Long-Term, Placebo-Controlled, Multicenter Study Evaluating the Safety and Efficacy of Obeticholic Acid in Subjects With Nonalcoholic Steatohepatitis
- AURORA: A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Capecitabine for the Treatment of Liver Fibrosis in Adults Subjects With Nonalcoholic Steatohepatitis
- A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of Encarsian, an Oral Capsopep Inhibitor, in Subjects With Decompensated Nonalcoholic Steatohepatitis (NASH) Cirrhosis
- A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study to Evaluate the Efficacy and Safety of Entacapone in Patients With Nonalcoholic Steatohepatitis (NASH) and Fibrosis
- A Phase 3 Double-Bind, Randomized, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Obeticholic Acid in Subjects With Decompensated Cirrhosis Due to Nonalcoholic Steatohepatitis
- A Phase 2 Dose-Ranging, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of ESP-305 in Subjects With Nonalcoholic Steatohepatitis (NASH)
- A Phase 2B Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of BMG-95038 (PEG-IFN-2b) in Adults With Nonalcoholic Steatohepatitis (NASH) and Stage 3 Liver Fibrosis
- A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of BMG-95038 (PEG-IFN-2b) in Adults With Nonalcoholic Steatohepatitis (NASH) and Decompensated Liver Cirrhosis

He also was lead investigator in the national WIN-R trial, which established the role of weight-based ribavirin dosing in the treatment of hepatitis C infection in African Americans.

Antiviral Therapy During Pregnancy Key to Preventing HBV Transmission at Birth

Preventing mother-to-child transmission (MTCT) of the hepatitis B virus (HBV) is recognized as one of the most effective strategies for eliminating HBV worldwide. However, management during pregnancy remains a challenge in countries with the highest infection rates, such as low-income areas of Africa and Asia.

In a comprehensive review, NYU Langone researchers propose a multipronged approach to managing patients during pregnancy based on viral load—the single most important risk factor for MTCT. Co-authored by James S. Park, MD, associate professor of medicine and director of the Asian Liver Health Program, and world-renowned researcher Calvin Q. Pan, MD, clinical professor of medicine, the paper recommends that women with HBV DNA levels above 200,000 IU/mL be treated with antiviral therapy during pregnancy. Their findings were published online in Hepatology International in October 2017.

Initiating antiviral therapy in late pregnancy can prevent failure of postnatal immunization in infants—which occurs in five percent to ten percent of cases when maternal HBV DNA levels exceed 200,000 IU/mL, they note. The failure rate is substantially higher, up to 30 percent, among mothers with high viral load.

Adopting a practical approach to reducing viral loads to under 200,000 IU/mL at delivery would be a major step toward eliminating HBV globally by 2030—the goal set by the World Health Organization (WHO), the authors state. In addition to HBV vaccination at birth, the WHO recommends the following strategies for eradicating MTCT:

- Universal screening of all pregnant mothers;
- Increased access to delivery in facilities with well-trained healthcare providers;
- Adopting a practical approach to reducing viral loads to under 200,000 IU/mL at delivery;
- Provision of early perinatal care to identify high-risk infants;
- Initiation of antiviral therapy in late pregnancy; and
- Development of novel therapies aimed at simplifying immunoprophylaxis regimens by decreasing the number of injections.

Growth in Liver Transplant Program

NYU Langone’s Liver Transplant Program offers complete medical and surgical care for a wide range of acute and chronic liver diseases. The program has tripled in size over the past two years and now offers both liver/heart and liver/kidney dual-organ transplantation.

The program includes a robust multidisciplinary group of hepatologists and liver cancer specialists from across NYU Langone, says Nabil Dagher, MD, associate professor of surgery, director of Abdominal Transplant Surgery, and director of the Transplant Surgery Fellowship. Dr. Dagher works closely with Dr. Park, medical director of transplant hepatology, and other specialists in surgical and medical oncology, pathology, and interventional and diagnostic radiology.

Specialists offer liver surgery related to hepatitis B and C, cholestatic liver disease, sclerosing cholangitis, acute fulminant liver failure, hepatocellular carcinoma, and biliary tract disorders. In addition to conventional surgery, physicians are skilled in the latest minimally invasive techniques, notes Dr. Dagher, including laparoscopic and robotic-assisted procedures.

“With a one-year patient survival rate exceeding 94 percent, our liver transplant program ranks among the top in New York State,” says Dr. Dagher, who works closely within the transplant team. “We are able to get the patient to liver function with a 90 percent survival rate at NYU Langone is one of the lowest in the state even though the program is transplanting some of the sickest patients. This is due to the excellent multidisciplinary care each patient is receiving, and growing initiatives to expand the organ donor pool. These include the living donor program and transplanting hepatic C-positive and HIV-positive donor livers.”

Disclosures: Ira M. Jacobson, MD, reported grant and research support from Assembly Biosciences, Bristol-Myers Squibb, Enanta Pharmaceuticals, GEMIT, Gilead, and Janssen. He is also a consultant/advisor for AbbVie, Amarin Pharmaceuticals, Assembly Biosciences, Gilead, Intercept, Janssen, Merck, Novo Nordisk, and Spring Bank Pharmaceuticals. Calvin Q. Pan, MD, is a speaker and consultant for Gilead. James S. Park, MD, is a speaker and consultant for Gilead.
New Era in Advanced Endoscopy

NYU Langone gastroenterologists and surgeons are at the forefront of using robotics and artificial intelligence (AI) to detect and treat gastrointestinal cancers. Members of this multidisciplinary team are collaborating to bring together their expertise in advanced endoscopy and minimally invasive colorectal surgery to deliver the best possible treatment to patients.

FLEXIBLE ROBOTIC SCOPE OFFERS ALTERNATIVE TO SURGERY

Seth A. Gross, MD, associate professor of medicine and director of clinical care and quality in the Division of Gastroenterology and Hepatology, and Mitchell A. Bernstein, MD, professor of surgery and director of colorectal surgery, were among the first doctors in New York State and among the first in the country to use the new endoscopic Flex Robotic System (Medrobotics) in the gastrointestinal tract. Using a robotic platform, the team removed a large premalignant rectal lesion in a patient who was discharged home the same day.

The procedure involves inserting a flexible scope into the anus while the patient is under general anesthesia. Using a robotic console, physicians snake the illuminated endoscope to the site of the lesion, where a high-definition, three-dimensional camera provides a clear view of the patient’s anatomy. Physicians navigate the robotic scope to a position in front of the target lesion and then dock it to establish a stable platform, says Dr. Gross. The procedure instruments are then inserted down the side ports until they become visible in front of the camera.

"The technique is particularly effective for removing large precancerous lesions in the lower colon," Dr. Gross explains. "These lesions are challenging to remove using conventional colonoscopy and traditionally may require abdominal surgery."

The flexible robotic scope gives us the ability to work effectively in a very tight space. The articulating arms of the robot allow us to perform surgical techniques from an endoscopic point of view."

—Seth A. Gross, MD
**New Era in Advanced Endoscopy**

“This flexible system is also being used to treat rectal cancer,” says Dr. Bernstein. For example, NYU Langone physicians are currently using it in transanal total mesorectal excisions (TME), which involve excising the anus through the rectum rather than cutting through the pelvis.

“The flexible scope overcomes the limitations of laparoscopic instruments, which are difficult to maneuver in the narrow confines of the pelvis,” adds Dr. Bernstein.

“We are one of the very few centers doing transanal TME to treat rectal cancers,” he says. “Our flexible scope offers an exciting new platform that promises to enhance our ability to perform this innovative technique and improve patient care.”

**AI-ASSISTED COLONSCOPY**

Physicians are also evaluating emerging artificial intelligence (AI) tools to enhance detection of potentially cancerous lesions, says Dr. Gross. Computer programs loaded with tens of thousands of images of normal and diseased colons work to enhance conventional endoscopic procedures. Dr. Gross is a co-investigator in one of the first studies exploring whether real-time AI can help find polyps, not just in a computer lab, but in patients undergoing colonoscopy.

Now, before beginning an AI-assisted colonoscopy, Dr. Gross plugs his monitor into an AI-enabled computer. As he scans the area, the computer flags regions with potential abnormalities that merit further investigation.

“AI gives us an extra pair of eyes,” says Dr. Gross.

“It has the specificity and sensitivity to allow us to do a better surface inspection of the colon compared with conventional methods.”

The long-term potential for AI-enhanced procedures extends well beyond colonoscopy, Dr. Gross adds. For example, it might be used to better target areas with potentially precancerous changes for biopsy in patients at high risk of developing cancers of the gastrointestinal tract, such as those diagnosed with ulcerative colitis or Barrett’s esophagus.

“The AI-assisted technology offers great promise for enhancing the quality of our screening and diagnostic procedures, especially in the detection of precancerous and cancerous lesions,” says Dr. Gross.

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*Mitchell A. Bernstein, MD*
Recommended Publications

Published in: Gastroenterology.

Dr. Gross also served as the American College of Gastroenterology, the American College of Gastrointestinal Endoscopy, and the American College of Gastroenterology's American Board of Gastroenterology. He is the society's appointed representative, member of the I3 Summit task force, and co-chair of the artificial intelligence task force.

Prashant Sinha, MD, was a member of the conflict of interest; publications; and recognized as an expert in the field of gastroenterology.

In 2018, he was awarded the distinguished physician award by the Crohn's and Colitis Foundation of America.

Renee L. Williams, MD, MHPE, was named to the Board of Trustees of the American College of Gastroenterology. She is also chair of the Minority Affairs and Cultural Diversity Committee, American College of Gastroenterology.

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Tuition-Free Initiative Addresses High Student Debt

NYU School of Medicine announced in August 2018 that it will begin offering full-tuition scholarships to all current and future students in its MD degree program regardless of need or merit—a bold effort to simultaneously address the rising costs of medical education and still attract the best and brightest students to careers in medicine. “This decision recognizes a moral imperative that must be addressed, as institutions place an increasing debt burden on young people who aspire to become physicians,” says Robert T. Grossman, MD, the Saul J. Farber Dean of NYU School of Medicine and CEO of NYU Langone Health.

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