

# JOHNS HOPKINS InsideTract

NEWS FROM THE JOHNS HOPKINS  
DIVISION OF GASTROENTEROLOGY AND HEPATOLOGY

WINTER 2021



## Anne Marie Lennon Named Director of Division of Gastroenterology and Hepatology

Researcher and gastroenterologist Anne Marie Lennon unites cutting-edge research and clinical innovation.

The Johns Hopkins University School of Medicine announced in spring of 2020 that Anne Marie Lennon has been selected to serve as director of the Division of Gastroenterology and Hepatology.

Lennon's clinical work and extensive research as a bench scientist make her a natural fit for the position, says Mark Anderson, director of the Department of Medicine.

"It was a thrill and an honor to recruit Dr. Lennon to be the director of the Division of Gastroenterology and Hepatology," says Anderson. "She commands a rare constellation of accomplishments in cutting-edge, high-impact research, clinical care and leadership. Because of these traits, she was highly sought as a candidate to direct leading programs across our country."

Johns Hopkins offers the world's most comprehensive services around pancreatic care. And much of that care begins with a program Lennon has led for 11 years.

The Johns Hopkins Multidisciplinary Pancreatic Cyst Program gathers gastroenterologists, pathologists, surgeons and radiologists to observe images of patients' pancreatic cysts and map out paths for treatment or observation.

Much of Lennon's career has centered on not just finding and treating, but also preventing pancreatic cancer.

In 2019, Lennon was part of a team that published a journal article that could herald a new approach to managing pancreatic cysts.

Though the great majority of pancreatic cysts do not become cancerous, current practice follows a better-safe-than-sorry approach: "When in doubt, resect."

"A patient might undergo surgery who doesn't truly need it," Lennon says. "The surgery itself is tough and has the potential for some complications that can really affect quality of life. It's great when we can avoid that."

Lennon and her co-authors developed "CompCyst," artificial intelligence that considers millions of genetic combinations and helps physicians predict which pancreatic cysts are more likely to turn cancerous.

A year before the CompCyst publication, the journal *Science* published an article by Lennon and the research team detailing a blood test that can detect proteins and gene mutations from eight common cancers that account for two-thirds of all U.S. cancer deaths.

The research studied blood samples from more than 1,000 patients with nonmetastatic, stages I to III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung and breast. The median overall sensitivity, or the ability to find cancer, was 70% and ranged from a high of 98% for



Much of Anne Marie Lennon's career has centered on finding, treating and preventing pancreatic cancer.

ovarian cancer to a low of 33% for breast cancer.

For the five cancers that have no screening tests — ovarian, liver, stomach, pancreatic and esophageal cancers — sensitivity ranged from 69% to 98%. The test was performed on 812 healthy people and produced only seven false-positive results.

Lennon regularly publishes with many of the top cancer researchers in the field, including Johns Hopkins colleagues Bert Vogelstein, Michael Goggins, Nick Papadopoulos and Ralph Hruban.

A native of Ireland, Lennon joined the Johns Hopkins faculty in 2010, following a two-year fellowship in advanced ultrasound and endoscopic

retrograde cholangiopancreatography.

After earning her medical degree in 1996 from Dublin's Royal College of Surgeons, Lennon received a Ph.D., from the National University of Ireland.

In addition to her title of professor of medicine, Lennon is also a professor of oncology, radiology and surgery. She is a member of the Johns Hopkins Gastric Cancer Center, the Von Hippel-Lindau Clinical Care Center and the Sol Goldman Pancreatic Cancer Research Center. ■

To contact the Division of Gastroenterology and Hepatology, please call 410-933-7495.



# Destigmatizing Liver Transplant for Patients with Alcohol Use Disorder

Johns Hopkins is one of the few centers in the United States that regularly transplants livers into patients with alcohol-related liver disease whose sobriety doesn't reach six-month threshold.

**H**epatologist Victor Chen and colleagues at Johns Hopkins want to change the way Americans think about alcohol use disorder and liver transplants.

For decades, transplant centers in the United States have followed a practice that requires patients to abstain from drinking alcohol for six months to be eligible for a liver transplant.

With cadaveric donor livers in high

demand, most transplant centers put patients whose liver damage stems from active alcohol use at the bottom of their priority lists — if they consider them at all. No matter the severity of the liver disease or how long the patient is expected to survive without a transplant, the majority of U.S. centers will not perform the procedure.

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related liver disease whose sobriety doesn't reach the six-month threshold.

Chen believes what puts Johns Hopkins ahead of most American transplant centers in this area is the collaboration between hepatologists, surgeons, social workers and addiction specialists.

“We use a combination of behavioral therapy and medicine to help people avoid alcohol after transplant,” he says.

Chen says that, when he talks to medical students about the approach, many of them cannot understand why the policy would be controversial.

“A lot of times, I'll get this look from them that says, ‘why are we even talking about this?’”

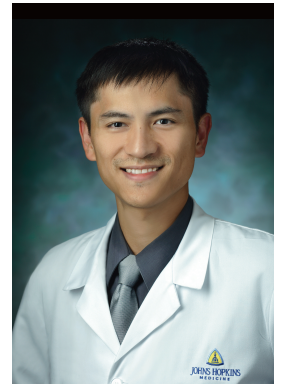
In 2011, a European team of hepatologists challenged the notion of the six-month sobriety policy. Soon after, the practice of transplant for patients with alcohol-damaged livers became more common across the continent.

But in the United States, the policy remains the norm.

“We were one of the very first transplant centers in the nation to say ‘maybe there's something to this,’” says Chen. “We started exploring and incorporating it into our own culture.”

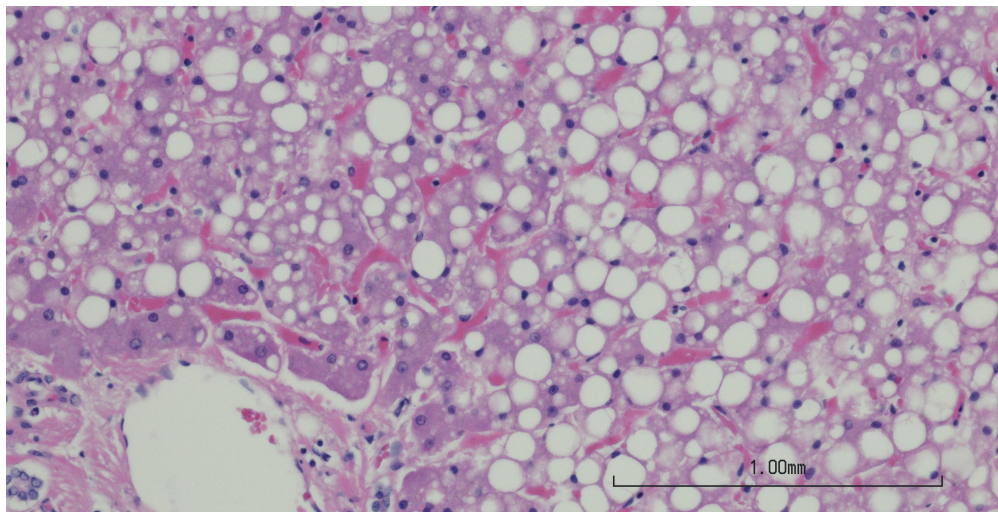
Today, according to Chen, Johns Hopkins performs about 25 liver transplants

*(continued on back cover)*



“WE USE A COMBINATION OF BEHAVIORAL THERAPY AND MEDICINE TO HELP PEOPLE AVOID ALCOHOL AFTER TRANSPLANT.”

—VICTOR CHEN



Johns Hopkins performs about 25 liver transplants a year for patients who would not otherwise get the lifesaving surgery. Image shows macrovesicular hepatic steatosis of the liver.

OGPHOTO/GETTY IMAGES

## IDEAS AT WORK

### Johns Hopkins Develops Tiny Machines That Deliver Medicine to the Intestines

Invented by biomedical engineer David Gracias and gastroenterologist Florin Selaru, “theragrippers” are devices that clamp onto intestinal mucosa and release medicine.

Inspired by a parasitic worm that digs its sharp teeth into its host's intestines, Johns Hopkins researchers have designed tiny, star-shaped micro-devices that can latch onto intestinal mucosa and release drugs into the body.

David Gracias, a professor in the Johns Hopkins University Whiting School of Engineering, and gastroenterologist Florin Selaru, director of the Johns Hopkins Inflammatory Bowel Disease Center, led a team of researchers and biomedical engineers that designed and tested shape-changing machines that mimic the way the parasitic hookworm affixes itself to an organism's intestines.

Made of metal and thin, shape-changing film and coated in a heat-sensitive paraffin wax, “theragrippers,” each roughly the size of a dust speck, potentially can carry any drug and release it gradually into the body.

The team published results of an animal study in October as the cover article in the journal *Science Advances*.

Selaru says that extended-release drugs often make their way entirely through the gastrointestinal tract before they've finished dispensing their medication.

“WE'VE BEEN WORKING TO DEVELOP SMALL DRUG CARRIERS THAT CAN AUTONOMOUSLY LATCH ONTO THE ORGAN AND KEEP THE DRUG LOAD INSIDE THE GI TRACT FOR A DESIRED DURATION OF TIME.”

—FLORIN SELARU

“Normal constriction and relaxation of GI tract muscles make it impossible for extended-release drugs to stay in the intestine long enough for the patient to receive the full dose,” says Selaru, who has collaborated with Gracias for more than 10 years. “We've been working to solve this problem by designing these small drug carriers that can autonomously latch onto the intestinal mucosa and keep the drug load inside the GI tract for a desired duration of time.”

Thousands of theragrippers can be endoscopically deployed in the GI tract. Once released, the machines migrate to the mucosal wall. When the grippers'



# Genetic Testing Reveals Important Clues in Unexplained Cases of Pancreatitis

For patients with recurrent acute or chronic pancreatitis, comprehensive genetic testing can help pinpoint the underlying cause of disease, avoiding potentially unnecessary tests and invasive treatments.

Johns Hopkins gastroenterologist Elham Afghani sees many patients whose pancreatitis has been diagnosed as idiopathic or unexplained. “A lot of them are told there’s nothing that can be done for them,” says Afghani. “By the time they decide to come to Johns Hopkins, they’re frustrated with ongoing episodes of acute pancreatitis or abdominal pain.”

But a growing field of research is providing clues to this mysterious condition. In the past few years, she says, genetic testing has revealed gene mutations that increase the risk of pancreatitis and are commonly found in patients with unexplained pancreatitis. The discovery of these genes has changed the way Johns Hopkins gastroenterologists approach the condition.

Afghani says that genetic testing has contributed to the Johns Hopkins team’s ability to identify the origins of a patient’s disease.

“We’ve seen a significant drop in the number of pancreatitis cases that are idiopathic,” says Afghani. “We’re getting a lot more clarity, and it’s a great feeling to help patients get to the bottom of this problem.”

Many different conditions can lead to painful inflammation of the pancreas. Afghani says the first goal is to determine the underlying cause.

“Comprehensive genetic testing is done once all other major common etiologies have been excluded. Most patients with pancreatitis have both environmental and genetic contributions to their disease. Knowing whether genetic mutation is a factor can save patients from undergoing a lot of tests that can be difficult.”

For instance, endoscopic retrograde cholangiopancreatography [ERCP], while vital in certain circumstances, can sometimes aggravate bouts of pancreatitis when used as a diagnostic tool.

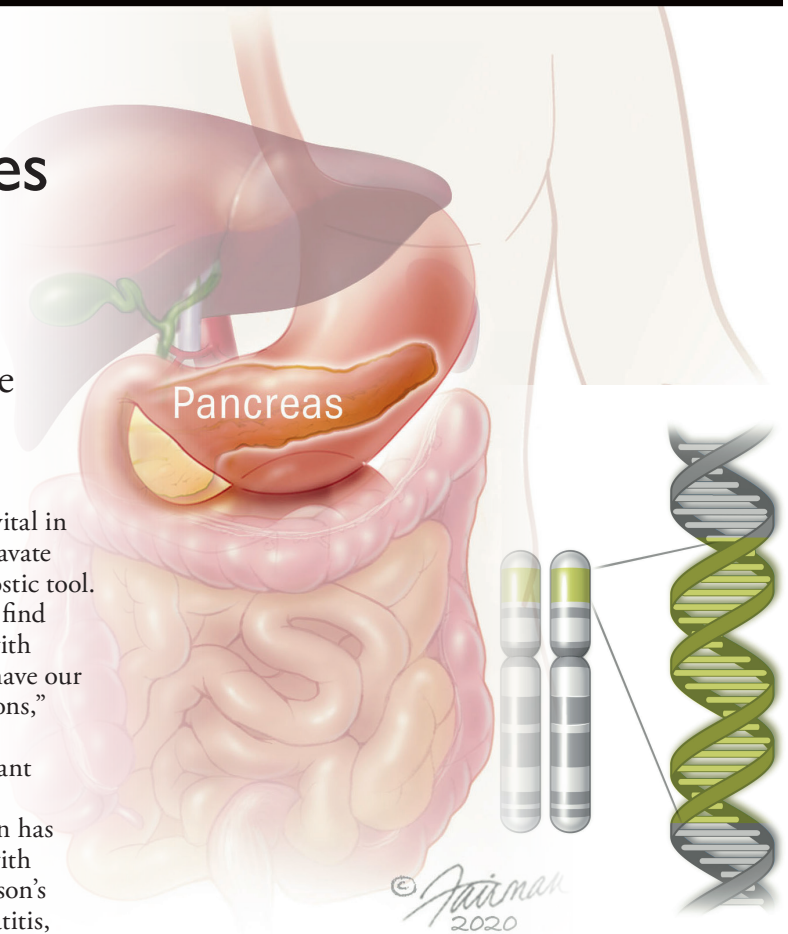
“If we can look at a genetic workup and find a mutation of one of the genes associated with recurrent or chronic pancreatitis, then we have our answer and can move on to treatment options,” Afghani says.

The testing can also reveal other important determinants of health.

“For example, knowing whether a person has a mutation of one of the genes associated with pancreatitis can help us determine that person’s risk of developing complications of pancreatitis, including diabetes, exocrine insufficiency and, in some, pancreatic cancer,” says Afghani, adding that knowing about hereditary risk can also benefit a person’s family members.

For patients whose pancreatitis does not respond to treatment, the Johns Hopkins Pancreatitis Center offers a surgery where the pancreas is removed, and the insulin-producing cells are harvested from the pancreas and transplanted to the patient’s liver, where they can continue to produce insulin. The multidisciplinary Total Pancreatectomy and Islet Autotransplantation Program brings together gastroenterologists, endocrinologists, radiologists and surgeons to make sure the transplantation succeeds. ■

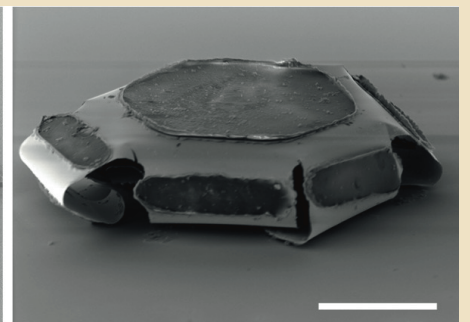
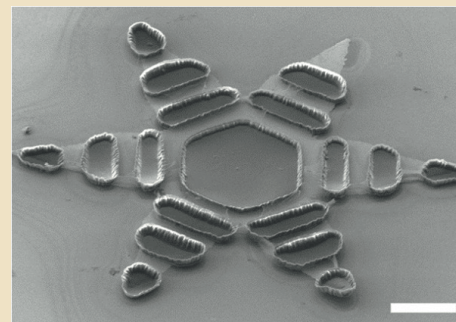
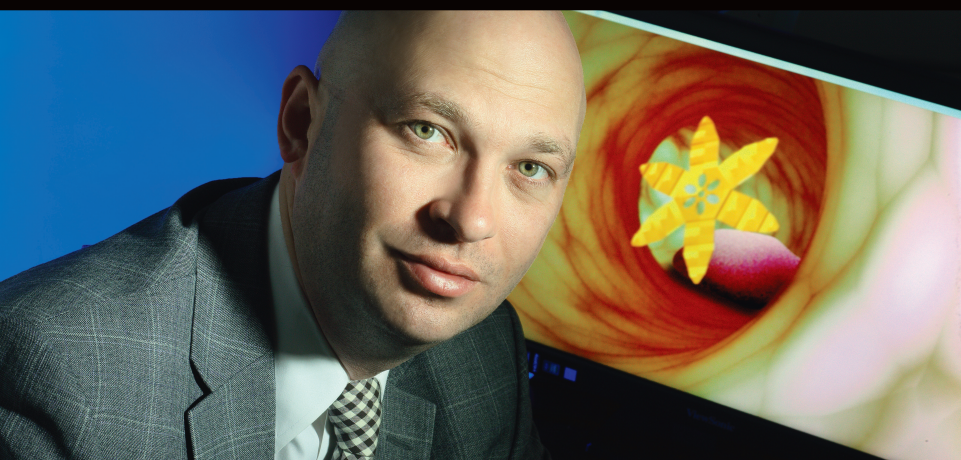
To refer a patient or request an appointment, call 410-933-7495.



Via genetic testing, Johns Hopkins gastroenterologists are increasingly better able to identify the origins of patients’ pancreatitis.

“KNOWING WHETHER A PERSON HAS A MUTATION OF ONE OF THE GENES ASSOCIATED WITH PANCREATITIS CAN HELP US DETERMINE THAT PERSON’S RISK OF DEVELOPING PANCREATIC CANCER.”

—ELHAM AFGHANI



Thousands of theragrippers can be endoscopically deployed in the GI tract. Once released, the machines migrate to the mucosal wall, where they release their medicine payloads gradually into the body. Image shows open and closed theragrippers.

wax coating reaches the temperature inside the body, the devices close autonomously and clamp onto the colonic lining. The closing action causes the tiny, six-pointed devices to dig into the mucosa and remain attached to the colon, where they release their medicine payloads gradually into the body. Within a day or two, the theragrippers lose their hold on the tissue and are

cleared from the intestine via normal gastrointestinal muscular function.

“We have seen the introduction of dynamic, microfabricated smart devices that can be controlled by electrical or chemical signals,” Gracias says. “But these grippers are so small that batteries, antennas and other components will not fit on them.”

Theragrippers, he says, don’t rely on electricity, wireless signals or

external controls. “Instead, they operate like small, compressed springs with a temperature-triggered coating that releases the stored energy autonomously at body temperature.”

The Johns Hopkins researchers fabricated the devices with about 6,000 theragrippers per 3-inch silicon wafer. In their animal experiments, they loaded a pain-relieving drug onto the grippers. The researchers’ studies found that the

animals into which theragrippers were administered had higher concentrations of the pain reliever in their bloodstreams than did the control group. The drug stayed in the test subjects’ systems for nearly 12 hours versus two hours in the control group. ■

To learn more about this research or refer a patient, call 410-933-7495.

## Destigmatizing Liver Transplant for Patients with Alcohol Use Disorder

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a year for patients who would not otherwise get the lifesaving surgery.

Surgeon Andrew Cameron is chief of the Johns Hopkins University School of Medicine's Division of Transplantation and surgical director of liver transplantation.

He says that, while the six-month guideline isn't a factor at Johns Hopkins, candidates do need to meet certain qualifications. Among them is the patients' insight into their own alcoholism.

"This is for people for whom there is evidence of an ability to turn their life around," Cameron says. "Before we agree to the transplant, we look at the patient's family or other support systems and the patient's commitment to change."

Funders have taken note of the work taking place at Johns Hopkins. Last year, Cameron received an \$8.4 million grant from the National Institutes of Health to study alcoholic hepatitis. Chen also secured an NIH grant that began in July 2020. His five-year, \$1 million funding supports research into transplant candidate selection for alcohol-related liver disease.

Part of Cameron's funding allows his team to explore solutions to help transplant patients avoid a recurrence of the condition. "A liver transplant won't cure alcohol use disorder," Cameron acknowledges. "We're exploring behavioral and pharmacologic interventions to give our patients their best shot at a healthy life." ■

To refer a patient, call 410-933-7495.

### CONTACT INFORMATION

Gastroenterology Central  
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410-933-7495

The only number you need to refer any patient to any Johns Hopkins GI service.

Gastroenterology and Hepatology  
Division Website  
hopkinsmedicine.org/GI

Hopkins Access Line (HAL)  
Your 24/7 connection to Johns Hopkins full-time faculty members in any subspecialty: 410-955-9444 or 800-765-5447.

Online Referral Directory  
Find a Johns Hopkins physician by name, specialty and more at hopkinsmedicine.org/profiles.

## JOHNS HOPKINS InsideTract

Inside Tract is one of many ways the Johns Hopkins Division of Gastroenterology and Hepatology seeks to recognize and enhance its partnership with its thousands of referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome.

This newsletter is published for the Division of Gastroenterology and Hepatology by Johns Hopkins Medicine Marketing and Communications.

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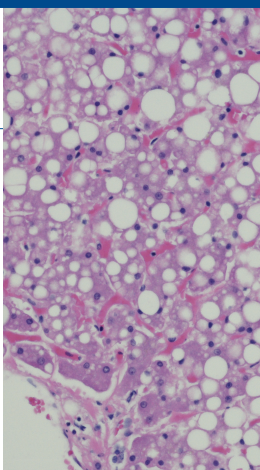
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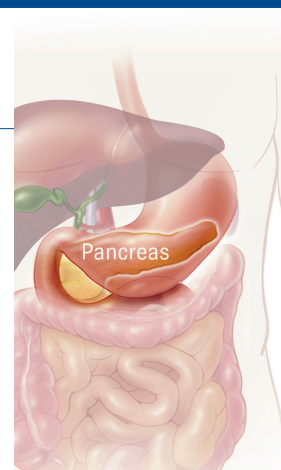
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