AUGUST 2019

Cleveland Clinic

Family Matters

INFORMATION FOR PEOPLE WITH COLORECTAL CANCER IN THEIR FAMILIES
Published by the Sanford R. Weiss, MD Center for Hereditary Colorectal Neoplasia

Sheetz Family Funds New Specialty Training Fellowship

Cleveland Clinic is blazing another trail in health care, thanks to the generosity of a prominent Pennsylvania family.

The Sheetz family — owner of the Altoona-based mega convenience store chain of the same name — recently funded a new speciality training fellowship by donating $2 million to Cleveland Clinic's Sanford R. Weiss, MD Center for Hereditary Colorectal Neoplasia.

The James Church, MD, and Sheetz Family Endowed Clinical Fellowship in Hereditary Colorectal Cancer Syndromes is the first of its kind in the world and is anticipated to attract trainees from around the globe.

"I can't explain how incredibly important this donation is," says **Matthew Kalady, MD**, Weiss Center Director and Co-Director of the Cleveland Clinic Comprehensive Colorectal Cancer Program. "We have had a vision to create a fellowship like this for several years. There is a great need for education and expertise in hereditary colorectal cancer syndromes throughout the country.

"Cleveland Clinic, via the Weiss Center, has the premier team of physicians and caregivers for this condition. Through this fellowship, we will create a pipeline of doctors trained as new experts who will be able to serve these patients in new geographical areas. Also, they will be able to teach others, which will exponentially grow the quality of care for patients around the country. This is all made possible through the incredibly generous donation of the Sheetz family."

The cause is near and dear to the family, as four of eight Sheetz siblings were diagnosed with MYH Associated Polyposis (MAP) in 1985 by Cleveland Clinic colorectal surgeon David G. Jagelman.

MAP is an inherited disorder characterized by cancer of the large intestine (colon) and rectum.

"We each had about 300 precancerous polyps on our colon and we needed to have our colons removed in a surgery Dr. Jagelman identified as a total colectomy,"

The Sheetz family packaging 10,000 meals for Rise Against Hunger.

says Steve Sheetz, Sheetz Family Council chairman and one of the company owners. "Two other medical facilities said we needed an ileostomy (rerouting the small intestine outside the body to a collection bag); Dr. Jagelman said we did not. At the time, I was 37 years old, and my brothers were 29, 32 and 39. We were hoping we wouldn't have to have an ileostomy.

"We all had total colectomies and we have gone on to live normal lives. We are forever thankful for the care we received at Cleveland Clinic."

The family continues to choose Cleveland Clinic, now receiving treatment from Dr. Church and surveillance from the rest of the Weiss Team, as needed.

This is the family's first donation of such magnitude.

"We're honored to support Dr. Church in his efforts," Sheetz says. "He and the entire staff at Cleveland Clinic have been so good to us through the years and most likely saved our lives. I believe the fellowship will help save other lives as well."

The first doctor to go through the fellowship program will be **Mohammad Abbass, MD**, starting in August.

"Dr. Abbass was chosen not only because of his abilities, but also because of his tremendous interest in hereditary colorectal cancer syndromes," Dr. Kalady says. "He has been an outstanding colorectal surgery fellow at Cleveland Clinic. More importantly, he wants to make caring for these patients and families a big part of his career. His enthusiasm and interest, along with the structure of the program, will make it an unparalleled experience."

The fellowship is anticipated to further amplify the Weiss Center and Cleveland Clinic's reputation for attracting the best and brightest doctors.

"This program will also serve as a springboard from which the Cleveland Clinic education and influence will exponentially spread as the trainees go out in their workplace and train others in the Cleveland Clinic way," Dr. Kalady says. "The graduated trainees will be able to provide the best care to patients and families in their communities. It will continue to enhance Cleveland Clinic as a leader and innovator in health care."

Diagnosed with rare colon cancer syndrome, high schooler Kinzer Glanzer raises money for research.

Kinzer Glanzer was told he had signs of a rare hereditary colon cancer syndrome at age 17.

His mom, Tasha Perry, had him and his younger brother tested after learning the boys' father suffered from familial adenomatous polyposis (FAP).

Kinzer's dad sought treatment close to home in Sioux Falls, South Dakota, and ended up with an ileostomy, a procedure that reroutes the small intestine outside the body to a waste-collection bag.

Perry sought more for her son. That's how they ended up at Cleveland Clinic.

"My mom wanted me to go to the best of the best and she found they specialized in FAP," says Kinzer, now 18.

Perry chose Cleveland Clinic's Sanford R. Weiss, MD Center for Hereditary Colorectal Neoplasia after countless hours researching FAP.

"The conclusion was (Cleveland Clinic's) **Dr. Carol Burke** is the best of the best for treating patients with FAP," she said.

Kinzer had no symptoms, but a colonoscopy in Sioux Falls found 26 polyps, three of which were pre-cancerous.

The results were sent to the Weiss Centers nurse coordinator **Lisa LaGuardia, RN**, where its team of world-renowned experts in managing the syndrome determined that surgery would be required to remove his colon and/or rectum when the timing was right. An ostomy bag won't be required post-operation.

"He will get an annual colonoscopy until surgery and eventual surveillance of his upper gut also," says Center Director **Matthew Kalady, MD**. "If untreated, he has a 100 percent chance of getting colon cancer.

"If under appropriate surveillance and timely intervention, he can lead a full, relatively normal life."

And Kinzer fully intends to. The recent high school graduate will attend Mitchell Technical Institute in South Dakota and plans to intern at Lake Havasu Marina in Arizona as a boat mechanic. He currently details cars at a Chevy dealership in Mitchell.

"I like to work with vehicles or anything that's got wheels, I guess," he says.

He appears to have come to terms with his condition and is grateful to Cleveland Clinic. So much so that he raised hundreds of dollars for the Weiss Center at a high school basketball game.

His mom gushes with gratitude as well.

"The care received by all staff has been impeccable," she says. 'Taking the chance coming all the way from South Dakota to Cleveland in hopes of finding answers and treatment was very scary for all of us. From Weiss Center care coordinator Lisa LaGuardia, RN, to Dr. Burke, to Dr. Kalady, the nurses and everyone in between have just been outstanding. We have been truly blessed by all."

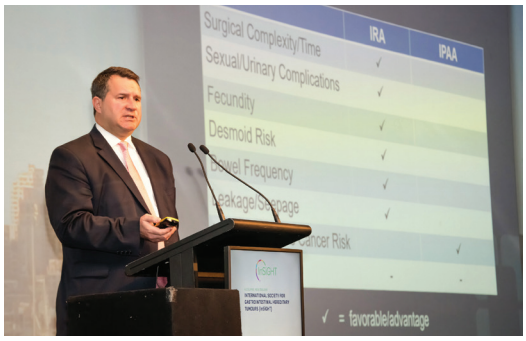
Dr. Kalady expressed appreciation and admiration for Kinzer and his family.

"It takes a lot of courage to deal with this diagnosis, and even more courage to get out there and talk about it and raise awareness," he explains. "We are extremely grateful for his efforts to raise awareness and raise money to help combat this condition."

2019 InSight Meeting in New Zealand

InSiGHT is the International Society of Gastrointestinal Hereditary Tumors, formed in 2003 from a blending of the Leeds Castle Polyposis Group and the International Collaborative Group on HNPCC. Its members are people who work in the field of hereditary gastrointestinal cancer, and include surgeons, gastroenterologists, geneticists, genetic counselors, registry coordinators, scientists, oncologists, psychologists and pathologists. Every two years InSiGHT holds a scientific meeting to present and discuss research and to learn about the latest developments in our understanding and treatment of the various syndromes that affect our patients. At The Weiss Center we find these meetings to be very stimulating and we learn a lot. We also have the opportunity to share our insight and our knowledge so that others can benefit.

This year the meeting was held in Auckland, New Zealand, the home city for Dr. Church. He was very happy to get the chance to visit family and friends, as well as to see the 8 other members of the Weiss delegation enjoying the sights and sounds and tastes of his country. Weiss was well represented in Auckland with 6 podium presentations, 12 poster presentations, and two invited lectures. Matthew Kalady was elected to the InSiGHT Council and James Church stepped down after many years of service. Dr. Church presented the Jagelman Oration InSiGHT did him the honor of adding his name to the title of the talk. In the future it will be the "James Church and David Jagelman Oration". Notable sessions at the meeting included discussions of Serrated Polyposis, Hereditary Diffuse Gastric Cancer, variation of presentation and the role of colonoscopy in patients with Lynch Syndrome, and the nuances of surgery in patients with Familial Adenomatous Polyposis. From what was presented, and from the shape of the discussions, there is no doubt that the staff of the Weiss center remain at the forefront of knowledge and understanding of the syndromes of hereditary gastrointestinal cancer. The next InSiGHT meeting will be in New York in 2021. We are already preparing for a leading role in this meeting.



The Weiss Delegation to InSiGHT 2019, Auckland, New Zealand. From left to right: James Church, Michael Cruise, Gautam Mankaney, Margaret O'Malley, Carol Burke, Brandie Leach, Lisa LaGuardia, Matthew Walsh, Matthew Kalady

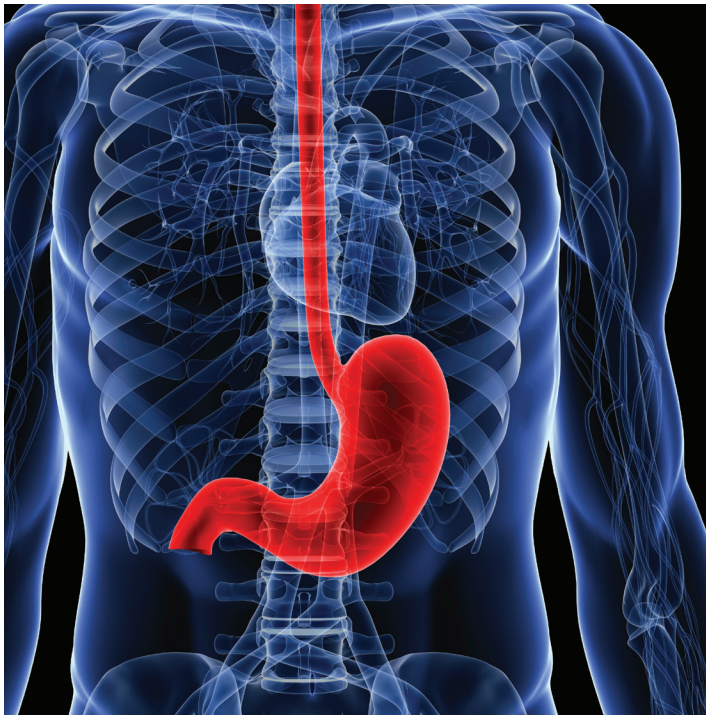
Helping our patients negotiate a diagnosis of a CDH1 mutation and the associated gastric cancer risk

Written by Carol Burke, MD

CDH1 is a gene that controls cell growth and death. When the *CDH1* gene is abnormal or mutated it results in a high risk of breast and stomach cancer. In the average risk United States population, breast cancer is common in women (12% risk) but stomach cancer is rare in men and women (<1% risk). When the *CDH1* mutation is not functioning correctly, the lifetime risk of cancer is extremely high including lobular breast cancer reported between 40-60% and stomach cancer at 40-67% in men and 63%-80% in women. The stomach cancer related to a *CDH1* mutation (also known as hereditary diffuse gastric cancer) is a special type of cancer that arises from cancer cells called signet ring cells (SRC). The Sanford R. Weiss, MD Center for Hereditary Colorectal Neoplasia has assembled a team of experts to care for patients with a *CDH1* mutation including registry care coordinators, genetic counselors, pathologists, psychologists, gastroenterologists, breast specialists, and surgeons. We feel a multidisciplinary team provides the best support, care and outcome for our patients and helps provide insights through our research into the cause, detection and prevention of *CDH1* related gastric cancer.

> "I take at least 77 random biopsies in four quadrants throughout stomach and also focus on performing targeted biopsies of subtle pale patches on the lining of the stomach."
>
> — *Carol A. Burke, MD*

Patients with a suspicious personal or family history of cancer undergo genetic testing to investigate if there is a hereditary component to cancer through the use of genetic blood tests. In patients with a *CDH1* mutation, there is a 50% chance of passing the gene on to children. Over the past decade, genetic testing has gone from testing a single gene to tests which include multiple genes that cause cancer. Many multi-gene cancer panel tests include the gene *CDH1*, and many patients without a personal or family history of stomach cancer are surprised when they are diagnosed with a *CDH1* mutation. Because the lifetime risk of SRC cancer in individuals with the *CDH1* mutation is as high as 80%, removal of the stomach is recommended to prevent cancer, usually between the ages of 18 and 40 years. The decision to remove the stomach is a substantial one but SRC cancer when advanced is deadly.



Before surgery, upper endoscopy with careful evaluation of the stomach and numerous biopsies to check for SRC cancer cells is done according to the Cambridge protocol which includes 25 random stomach biopsies. SRC cancer cells are not easily visible at the time of upper endoscopy because the cells are beneath the surface lining of the stomach. Detection rates of SRC cancer with endoscopic biopsy in the best of hands have yield SRC cancer detection rates of only 9-61% in patients with SRC cancer. Research led by gastroenterologist Carol A. Burke, MD, have modified the Cambridge screening protocol for SRC cancer, which yielded a 78% positive detection rate in the first nine asymptomatic patients who underwent upper endoscopy and then stomach removal. All cancers were early stage. "My approach in our patients at the Cleveland Clinic is to do more biopsies than recommended by the Cambridge protocol," she says. "I take at least 77 random biopsies in four quadrants throughout stomach and also focus on performing targeted biopsies of subtle pale patches on the lining of the stomach." Equally important to a careful endoscopist, is to have an expert gastrointestinal pathologist look at the biopsy specimens because SRC can be easily missed. Although the modified EGD exam does not require specialized training, Dr. Burke says that it is best to have the procedure performed by a detailed and experienced endoscopist at a specialized center, such as the Center of Excellence for *CDH1* which is housed within the Sanford R. Weiss, MD, Center for Hereditary Colorectal Neoplasia at Cleveland Clinic. Taking care of our patients and families with a *CDH1* mutation requires a multidisciplinary team which we have assembled at the Clinic."

Answers to your questions about nutrition and colorectal surgery.

Adapting to life after colorectal surgery can pose challenges when balancing nutritional needs. We asked Dr. Gail Cresci, Nutrition Researcher and Registered Dietitian and Director of Nutrition Research in The Center for Human Nutrition, for some advice on using nutrition to maintain digestive health.

I'm having colorectal surgery soon. What should I be eating or drinking before my surgery?

The Cleveland Clinic utilizes a protocol called Enhanced Recovery After Surgery (ERAS). The ERAS program is a set of steps patients and caregivers follow in the few days before and after surgery. A part of this protocol includes the recommendation to drink a liquid supplement containing several immune-modulating nutrients including omega 3 fatty acids, the amino acid arginine and nucleic acids 5 days before and 5 days after surgery. This supplement is available without a prescription and available at Cleveland Clinic pharmacies or via the internet.

Studies have shown that patients who follow this protocol experience decreased nausea and pain, quicker return of bowel function, improved wound healing, earlier hospital discharge, and fewer hospital re-admissions and postoperative complications. You should discuss with your doctor whether the ERAS protocol is right for you.

How about after my surgery?

When your doctor gives you the ok to start eating food after surgery, start off with soft foods low in roughage that are easy to digest for the first 2-3 weeks after surgery, and make sure to eat slowly, avoid overeating, and to chew foods thoroughly. To help regulate bowel movements, try to eat regularly with 5-6 small meals daily and eventually at least 3 meals per day. Gradually add fiber back into your diet and avoid fried greasy foods as much as possible. As you become better able to tolerate fiber, women should aim to consume 25-30 grams of fiber per day, and men 30-35 grams. If you have an ostomy bag, avoid foods that are not well-digested such as corn, nuts, seeds, popcorn, dried fruit, mushrooms, raw crunchy vegetables, meat casings, and salad greens.

It is very important to stay well-hydrated following surgery, and if you have an ostomy you may lose more body fluids. Instead of drinking a lot of water, try drinking fluids that contain small amounts of sugar and salt. Pedialyte or low-calorie sports drinks (for example, Gatorade G2) 1 Liter with ½ tsp salt added should do the trick.

Should I take a probiotic for colon health?

Probiotics are live active cultures that have been shown to have beneficial effects on the gut microbiota. The gut microbiota is made up of trillions of microbes that aid in metabolism and digestion. Eating a balanced diet containing fruits, vegetables, and other sources of fiber helps to maintain a healthy microbiota. If diet is high in fat and sugar the gut microbiota composition shifts to less desirable microbes which produce non-beneficial metabolic byproducts.

Probiotic use may help in maintaining a healthy gut microbiota. However, beware of false advertising when shopping for a probiotic – many products have not been shown to have probiotic beneficial effects. Look for words on the label that specify the strain of bacteria used. Also, it is important to only use a probiotic that is labeled for a specific effect – there are probiotics designed for bowel regularity and others that help with immunity. So, if you are looking to help with regularity look for Lactobacillus bulgaricus, Streptococcus thermophilus, and Bifidus regularis. If you need to take an antibiotic and want to try to avoid diarrhea, look for products containing the strain Lactobacillus casei.

It is also very important to note that these products work mainly in the colon; so, if you've had most or all of your colon and ileocecal valve removed, taking probiotics may not be of much benefit to you, and may lead to bacterial overgrowth in the small intestine.

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When should I schedule a visit with a registered dietitian?

If you experience any of the following symptoms, a consultation in Nutritional Therapy may be beneficial. Appointments may be made by calling The Center for Human Nutrition at 216.444.3046. Virtual visits may be available.

- Unintended weight loss of 5% of your total body weight in one month, or 10% in 6 months.
- Difficulty chewing or swallowing
- Avoidance of certain foods because of gastrointestinal pain
- Persistent nausea

Resources

United Ostomy Associations of America, Inc (UOAA) **ostomy.org**
Coloplast US **coloplast.us**
Crohn's and Colitis Foundation **crohnscolitisfoundation.org**
Oley Foundation **oley.org**

Community Outreach

During the month of March (Colon Cancer Awareness Month) we reached out to the community to promote colon cancer education and screening. This was done through digital media, TV, radio or in person. Some of the highlights from March are included below.

Digital ads were sent through Facebook, Twitter, Instagram and Butts and Guts podcast: ClevelandClinic.org/buttsandguts

Amazon Alexa also had Colorectal Cancer-related Cleveland Clinic Tips of the Day

Colon cancer screening and education ads were in 19 local newspapers. Banners were on Carnegie Avenue, Regional Family Health Centers and The Terminal tower lobby promoting colon cancer awareness and screening

Staff attended the Cleveland Cavaliers basketball game to promote colon cancer outreach / screening education. Patients were recognized on the court at half time.

The outreach team worked with a barbershop for a colon cancer outreach / screening education program

Throughout the month interviews were done with our staff as well as patients who shared stories to promote colon cancer awareness.

Is Preimplantation Genetic Diagnosis (PGD) for me?

A big decision like PGD is highly personal, and how people make their choices is as individual as their DNA. Dr. Hurley, Weiss Center team psychologist had previously conducted a study that interviewed people with hereditary cancer risk about their attitudes towards PGD. The study showed that some felt positive about having access to the latest technology and a way to take control of their future. Others expressed religious objections to "playing God" or were concerned about interfering with the laws of nature. Some people felt that knowing about PGD meant that they should use it, to protect future children from harm caused by cancer risk. Others felt like they were coping with their risk, and could help their kids do the same: "What if my parents had PGD' ed me?" PGD can be expensive, which may affect other life plans like saving for a house or retirement. Trust that cancer treatments will be better in the future was a strong theme, but so was uncertainty. Sometimes after an in vitro fertilization cycle, the only embryos available to implant were the ones with the family mutation. It's important to explore all the angles to come up with a decision that reflects your personal values and goals.

To learn more about PGD contact The Genomic Medicine Institute at 800.998.4785"

CURRENT AND ENROLLING **STUDIES**

We are always looking for ways to help manage your disease. This may include any combination of procedures, medications, and lifestyle changes. As you know, preventative medications are limited, and as a hereditary cancer community, we want to help change that. We are excited to share trials that have been recently completed (results pending, stay tuned!), ongoing trials, and trials to come:

FAP – Combination therapy with DMFO (eflornithine) and Sulindac – The Cleveland Clinic was one of the enrollment centers for this trial through the Cancer Prevention Pharmaceuticals. Both DMFO and sulindac have been shown to prevent the formation of colon polyps. We recently completed enrollment for this trial, and the results will be out soon. Three groups will be compared –sulindac only, DMFO only, and the combination of both.

FAP – Erlotinib – Weekly therapy with erlotinib – We are actively recruiting for this trial through the Cancer Prevention Network. Erlotinib has been shown to reduce the number and sizes of duodenal polyps in FAP. This trial is evaluating the effects of weekly erlotinib therapy on duodenal polyps as well on colonic polyps. It is for adults with FAP who have stage II or III duodenal polyposis (ask us if interested, and we will tell you whether or not you qualify).

FAP – Guselkumab – Colon polyps form due to many reasons. Individuals with FAP are predisposed toward forming polyps due to DNA mutations that they are born with. Through life, they form polyps. Once the polyps form, they can be targeted through one of many mechanisms (DMFO and sulindac utilize different ones). Guselkumab targets one of the inflammatory pathways implicated in polyp formation. This trial is headed by Janssen Pharmaceutical Companies, and we hope to start enrollment for this trial in the very near future. It is for adults with FAP who have polyps in their pouch or rectum (ask us if interested, and we will tell you whether or not you qualify).

Lynch syndrome – Immunotherapy for rectal cancer – Stay tuned for more information on this trial. It is for those with Lynch syndrome who have developed a rectal cancer.

5th Annual Cleveland Undy Run/Walk

We are excited to share that the Colon Cancer Alliance and the Cleveland Clinic will be bringing back the 5th Annual Cleveland Undy Run/Walk on Saturday, September 28th at the East Bank of the Flats!

The Undy Run/Walk is about celebrating warriors currently fighting colon cancer, honoring survivors and paying tribute to those we've lost to the disease. By raising awareness about the importance of screening, we're saving lives.

We would like to share with you the 2018 Cleveland Undy results. We are pleased to announce that we raised over $100,000 and had 762 participants! A portion of the proceeds stay locally with the Cleveland Clinic though the Blue Hope Grant. Together, we are helping knock colon cancer out of the top 3 cancer killers.

We encourage you to join us or start a team for the race to help us support this cause.

ccalliance.org/events/2019-cleveland-undy-runwalk

The 7th Annual Hereditary Colon Cancer Day

The 7th Annual Hereditary Colon Cancer Day is set for September 13, 2019. The event will take place at the Cleveland Clinic Taussigg Cancer Center at 1 pm. Bring your family and join us for a day of free hereditary colon cancer education.

For more information and to RSVP, please call 216.444 6470. Space is limited.

Introducing New Team Members

Susan Milicia

Susan Milicia

Susan Milicia is the coordinator of the HNPCC/ Lynch Syndrome registry within the Sanford R. Weiss, MD, Center for Hereditary Colorectal Cancer. She received her associate's degree in nursing from Bryant & Stratton College and her bachelor of science in nursing from Western Governors University. Milicia joined Cleveland Clinic, Marymount Hospital, in 2012 and worked acute inpatient medical surgical nursing for past 7 years. She became ANCC Medical Surgical Nursing Certified in 2018. In December 2018, Susan joined the registry team.

Milicia is attracted by the mission of the Weiss Center, to prevent cancer and maintain a high quality of life in patients and families with hereditary colorectal cancer syndromes. She spends her free time with her fiancé and their three children ages 16, 15, and 12.

Amit Bhatt, MD

Amit Bhatt, MD

Amit Bhatt, MD is an advanced endoscopist who is delighted to be part of the Weiss Center Family. He is Cleveland Clinic trained, finishing his internal medicine residency, gastroenterology, and advanced endoscopy fellowship at the Clinic. During his training, thanks to grants from the American Society for Gastrointestinal Endoscopy (ASGE), and American College of Gastroenterology (ACG), Dr. Bhatt had the opportunity to train in Japan in learn advanced endoscopic resection and diagnostic techniques. Dr. Bhatt is excited to help serve the patients of the Weiss Center with these advanced endoscopic techniques.

Cleveland Clinic

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Recent Publications from the Weiss Center

Gene Expression Changes Accompanying the Duodenal Adenoma-Carcinoma Sequence in Familial Adenomatous Polyposis. Thiruvengadam SS[1], O'Malley M[2], LaGuardia L[2], Lopez R[3], Wang Z[4], Shadrach BL[4], Chen Y[5], Li C[5], Veigl ML[5], Barnholtz-Sloan JS[5], Pai RK[4], Church JM[2,6], Kalady MF[2,5,6], Walsh RM[2,7], Burke CA[2] *Clin Transl Gastroenterol.* 2019 June

Superior Mesenteric Artery Pseudoaneurysms in Patients With Familial Adenomatous Polyposis-Associated Intra-abdominal Desmoids: Case Series. Bolshinsky V[1], Xhaja X, Halleran DR, Church *J Dis Colon Rectum.* 2019 June

Endoscopic and histologic features associated with gastric cancer in familial adenomatous polyposis. Leone PJ[1], Mankaney G[2], Sarvapelli S[1], Abushamma S[1], Lopez R[3], Cruise M4, LaGuardia L[5], O'Malley M[5], Church JM[5], Kalady MF[5], Burke CA[6]. *Gastrointest Endosc.* 2019 May

Expert Commentary on the Diagnosis and Management of Lynch Syndrome. Kalady MF1. Dis Colon Rectum. 2019 April

Spigelman stage IV duodenal polyposis does not precede most duodenal cancer cases in patients with familial adenomatous polyposis. Thiruvengadam SS[1], Lopez R[2], O'Malley M[3], LaGuardia L[3], Church JM[4], Kalady M[4], Walsh RM[5], Burke CA[6] *Gastrointest Endosc.* 2019 February