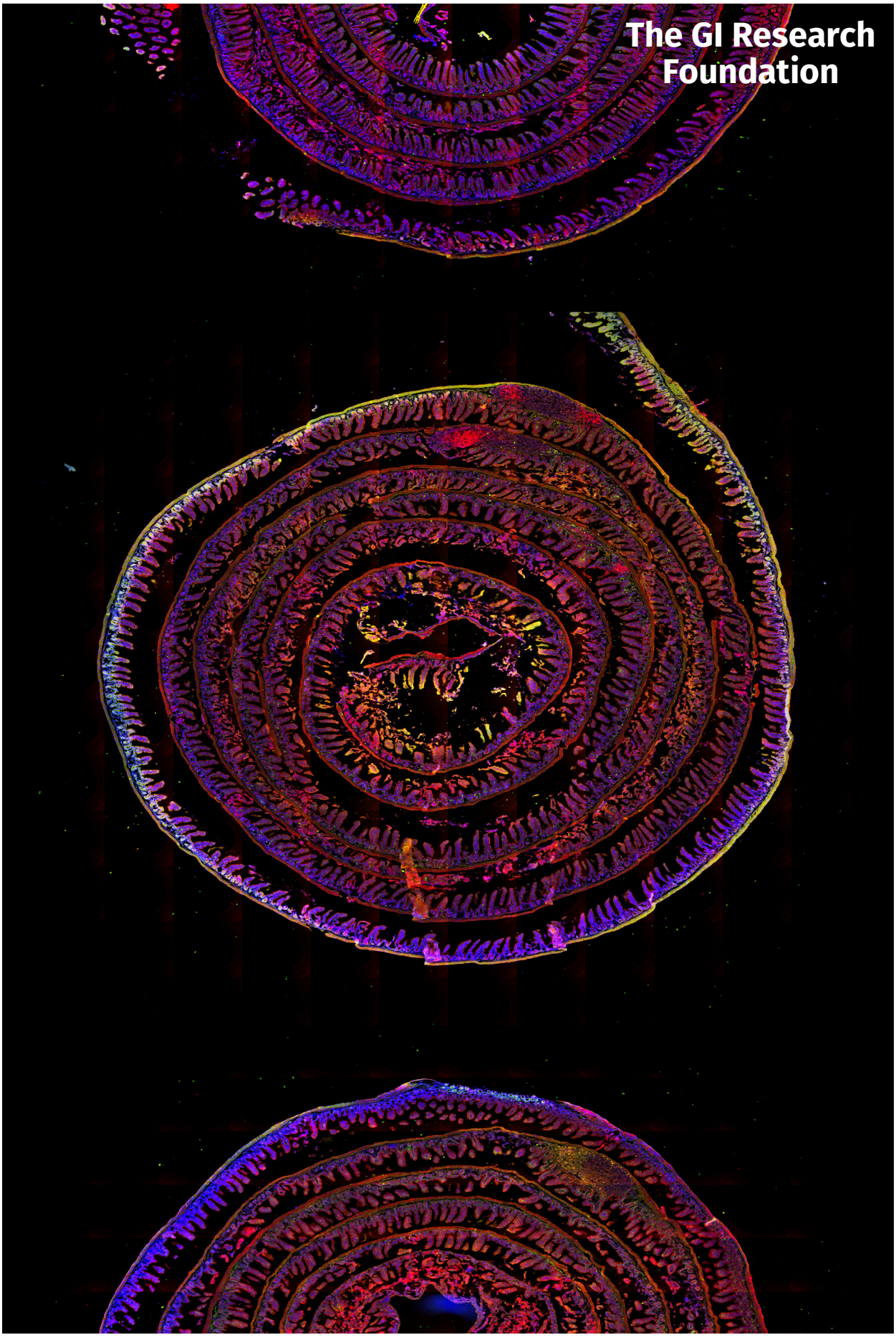
2022 In Review



The GI Research Foundation

The GI Research Foundation (GIRF) is a 501(c)3 non-profit organization dedicated to raising funds to support the physicians and scientists at the University of Chicago Medicine Digestive Diseases Center in their efforts to provide outstanding care, train future leaders, and perform innovative clinical and laboratory research in order to treat, cure, and prevent digestive diseases.

CONTENT

FRONT COVER: Photo of three sections of mouse ileum, the most distal part of the small intestine, that have been stained with immunofluorescent antibodies to create the beautiful contrasts you see. This photograph was created by Amelia Davis, the Lab Manager at the Abadie Lab at UChicago Medicine. One focus of study in this lab is the role of B cells (seen in red) in the pathology of celiac disease, a chronic immune disorder triggered by gluten ingestion. It results in damage of intestinal lining and causes diarrhea, fatigue, weight loss, bloating and anemia. This specific study seeks to better understand the causes of tissue damage at the cellular level. Enhanced understanding of B cell antigen presentation may also shed light on other diseases such as rheumatoid arthritis, multiple sclerosis, and type 1 diabetes.

The GI Research Foundation continues to be inspired by its founder, Dr. Joseph B. Kirsner and center patient outcomes in its research funding.

My principal mission became excellence in the care of the patient; the patient was the goal in everything we did. If we did research, it would eventually evolve into a therapeutic procedure, a better way to take care of a particular problem, and the patient would benefit.

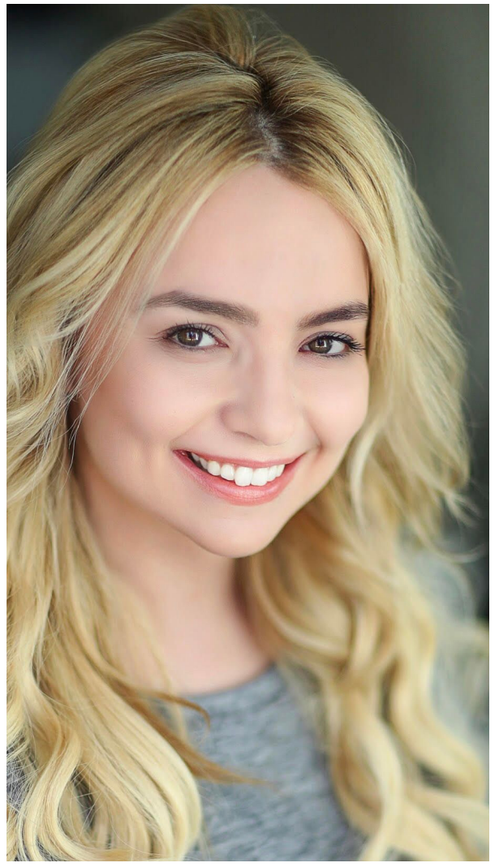
I do want to express my appreciation and respect to the men and women of GIRF, all of them. They are doing this voluntarily. . . The fact that they are so liberal in their association and support is a great honor for us and I express the sentiments of not only my colleagues in gastroenterology but also the University of Chicago. GIRF is held in the highest regard throughout the country.

JOSEPH B. KIRSNER, MD, PhD
1909-2012

LEADERSHIP
Yekaterina Chudnovsky, President
Kathryn Karmin Shafer, Executive Vice President
Jackie Casey, Executive Director

GIRF 2022

Your Research Learning Journey



- Initiated an annual competitive grant process awarding over $1 million to nine novel studies at the University of Chicago Medicine.
- Invested in critical technology and equipment that fuels research breakthroughs.
- Educated our constituents through Moving the Needle—our annual research spotlight event, Visceral—a new GI Research Foundation podcast, and a three-part webinar series.
- Celebrated together with three Balls—two virtual and one hybrid.
- Golfed with sports legends at the Larry A. Pogofsky All Star Challenge.
- And continue unparalleled support of the UChicago Medicine Digestive Diseases Center physician-scientists.

I invite you to read these pages featuring highlights from a successful 2022—achievements made possible with your support.

Reflecting on our accomplishments, I recognize how much work is left to do. I look forward to supporting the GI Research Foundation mission as Board Chairperson and continuing our quest for digestive diseases patients all over the world.

Together, let us continue to change lives.

Katie Chudnovsky
Board President, 2020-2022

Dear Friends,

When I first gaveled in as Board President in January 2020, the GI Research Foundation began its 59th year of fighting for digestive diseases patients. Our goals were significant, with plans to expand research funding and move closer to finding cures.

Thanks to our steadfast Board of Directors and volunteers, dedicated scientific partners at the University of Chicago Medicine Digestive Diseases Center, and devoted donors and friends, our commitment has never been stronger. Over the past three years, we discovered new opportunities to connect with and grow our community, while sustaining our existing operations.

- Launched CA CURE—a courageous initiative to change how we treat digestive cancers, with a focus on immunotherapies and vaccines.

Why GIRF

DAVID T. RUBIN, MD

The Joseph B. Kirsner Professor of Medicine
Lead Scientific Advisor, GI Research Foundation
Chief, Section of Gastroenterology, Hepatology, and Nutrition, The University of Chicago Medicine was honored with Joseph B. Kirsner Award at the 2022 GIRF Ball.

The following is excerpted from his remarks that evening.

How do you create a culture of inquiry, an expectation for new discoveries, and significant results for patients and their families? How do you expand expectations from 'managing disease symptoms' to an expectation that patients' quality of life should be unconstrained by their diseases?

The ingredients that have made the Digestive Diseases programs at the University of Chicago great are 1) the University itself, 2) our brilliant and dedicated faculty and staff, and 3) the amazing GI Research Foundation. It is these special ingredients that are the theme of my remarks.

The University of Chicago was created as an institution of higher learning with, as University President Robert Maynard Hutchins said in 1931 “devotion to truth, the courage to be independent, an enthusiastic interest in the community and in new ideas, in intellect rigorously trained, and being trained.”

Our medical center grew out of the University and was developed with the same principles. The medical center has been a part of the campus for almost 100 years, and the core function of the University of Chicago Hospitals required commitment to the community and patient care but always emphasized research to understand the mysteries of the human body. Among its first eight faculty hires was Dr. Walter Palmer, a physician scientist and son of a family practice doctor who had an interest in GI diseases. Dr. Palmer focused on research and discovery of the major GI problem of the day—peptic ulcer disease. In 1935, Palmer was joined by and then mentored a young physician, Dr. Joseph Kirsner. Shortly after starting his job with Palmer, Kirsner met a young woman with ulcerative colitis. A little-known condition at that time, she succumbed from her disease, and this had a profound impact on Kirsner. He subsequently devoted his career to understanding the causes and treatments for the inflammatory bowel diseases.

By now, the legacy of Kirsner is known to many of you— it is the reason the GI Research Foundation came to exist. As clinicians, we all have learned how such experiences with our patients deeply affect us, every day.

The second ingredient to our ongoing success is our UChicago people. Our amazing Digestive Diseases Center is now made up of over 300 physicians, scientists, trainees, nurses and staff. In the last year we have been in more locations, seen more patients, performed more surgeries and published more scientific papers than ever before. Under the co-directorship of Mike Charlton and John Fung, our transplant center has performed more transplants in multiple organs than in the history of the institution.

We have a multi-disciplinary liver tumor clinic led by Dr. Anjana Pillai, our multi-disciplinary obesity initiative led by Dr. Mustafa Hussain, our cutting-edge interventional endoscopy program led by international leader Dr. Uzma Siddiqui, and most recently, our intestinal ultrasound program, led by Dr. Noa Krugliak Cleveland that enables us to assess inflammation in the bowels in real time at the bedside. Our research teams have been incredibly productive as well, with over 300 active human subject trials and hundreds of ongoing pre-clinical laboratory experiments, with critical contributions from Valerie Abadie, PhD; Luis Barreiro, PhD; Eugene B. Chang, MD; Bana Jabri, MD, PhD; Ed K. McDonald, IV, MD; Neil Hyman, MD; Sonali Paul, MD; Joel Pekow, MD; Carol Semrad, MD; Benjamin Shogan, MD; and Kinga Skowron-Olortegui, MD, among many others, all of which you learn about through the GI Research Foundation's communications throughout the year.

But at the end of the day, it still comes back to the individual physician, the individual scientist, and their focus on the next individual patient, in an increasingly difficult and competitive environment.

Which brings me to our third ingredient: The GI Research Foundation. You, our friends at the GI Research Foundation, have stepped up time and again to address the needs of the physicians and scientists, and in the last 8 years we have been privileged to work with you to expand support to meet the demands of these times.

An institution like the University of Chicago and its multitalented scientists and experts across different departments and specialties is the only place a program like this can be created and succeed, and with GIRF’s help, I know we will.

Your support is critical to our missions. We appreciate your dedication and generosity. Thank you.

Research Funding Strategy

JACKIE CASEY, EXECUTIVE DIRECTOR

For the past several years, under the wise guidance of our scientific advisors, the GI Research Foundation (The Foundation) has honed its approach to research funding. The strategy has become more sophisticated and the dollars for awards have grown. In fiscal year 2022 (July 1, 2021 to June 30, 2022), the Foundation awarded just over $1.5 million in research grants. From July 1 through the end of calendar year 2022, we have awarded over $19 million. This stunning growth is the result of donors like you at all levels of giving: investing in research and directed donations, helping us to launch important new grantmaking initiatives.

The Foundation's strategy funds research from discovery in the lab to the patient's bedside. Research is hope. With each grant request, we ask, "How will this, or how could this, improve patient outcomes and eliminate suffering?"

The Foundation's funding strategy supports research across the disease spectrum, from understanding the causes of disease, to ensuring accurate diagnosis and successful treatment and disease monitoring, to discovering prevention pathways, and finally, developing cures.

The grantmaking strategy evolves with new scientific breakthroughs and lessons learned, and centers on scientific partnership, especially with our long-time partner, the University of Chicago Digestive Diseases Center.

PARTNERS IN RESEARCH

GI RESEARCH FOUNDATION

AT THE FOREFRONT UChicago Medicine Digestive Diseases Center

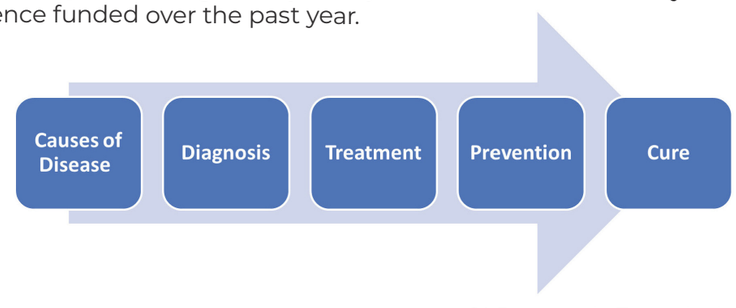
With each grant request, we ask, "How will this, or how could this, improve patient outcomes and eliminate suffering?

GRANTS FUNDING STRATEGY:

- An annual competitive grant review process evaluates proposals from investigators and physician-scientists at the University of Chicago who are working across the digestive disease states (i.e., Crohn's, ulcerative colitis, Celiac, etc.) and across the research spectrum from laboratory discoveries to clinical applications.
- Based on the knowledge that ground-breaking research needs best-in-class facilities and state-of-the-art equipment to achieve desired results and attract world-class scientists, we provide critical capital funding that is almost impossible to get from traditional medical research funders.
- Based on the belief that building a diverse scientific field is key to sustaining the research pipeline, our early career awards seek to nurture young investigators, inviting bold new ideas.
- Knowing that communities of color face challenges accessing prevention and care strategies for digestive diseases, we make specific grants using innovative strategies to address these challenges and disparities.
- With donor-directed grants, the Foundation launched CA CURE, with a focus on digestive system cancer cure research (specifically immunotherapies and personalized vaccines). Using a competitive proposal process, project ideas from leading scientists across the country, including human clinical trials, were funded in 2022.
- The Foundation is launching a second special initiative in regenerative medicine, a groundbreaking approach to healing that seeks to use the body's own cells and tissue. Several initial grants in this area of science were made in 2022.

Carefully stewarding our donor dollars, the Foundation is often a first-in funder, providing critical early support of novel and innovative pilot studies and core support of critical research needs. These early dollars often yield the research results needed to attract more traditional and larger donors.

Connecting our constituents to the research strategy is a key part of the GI Research Foundation's mission. Understanding research is a journey anyone can take. In this *Year in Review*, you can begin this journey with us as we introduce you to the incredible science funded over the past year.



CA CURE 2022

A New Initiative to Cure Digestive-Tract Cancer

Despite centuries of research, treating and curing cancer remains an urgent health research priority. Far too many people at younger and younger ages are diagnosed with fatal cancers, often after living with a digestive disease such as Crohn's, ulcerative colitis, fatty liver disease, and others. Despite its prevalence, colon cancer research is grossly underfunded.

With extraordinary and transformational support from anonymous donors, the GI Research Foundation launched a bold initiative, CA CURE, to identify and fund research to improve diagnostics and develop immunotherapies and personalized vaccines.

In 2022, CA CURE sought projects that might have difficulty attracting funds because they are too experimental or are in the initial stages of development. With a focus on improving patient outcomes, we funded nine rigorously evaluated research projects from across the country. In its initial phase, CA CURE put vital research dollars in the hands of leading scientists. Thanks to the expert scientific review from eight physician-scientists and investigators at the University of Chicago, Yale University Medicine, Weill Cornell Medicine, and MD Anderson, the GI Research Foundation developed a scientifically robust review process.

In just five months, the Foundation awarded $18,421,770 in grants.

This has been an extraordinary team effort, demanding time, expertise, and wisdom from many. The GI Research Foundation is so fortunate to have scientific leaders who care about our success and lay leaders with the passion to immerse themselves in learning complicated research.

The GI Research Foundation looks forward to sharing the results of these projects with you in the coming months and years.

$18,421,770

in Groundbreaking Research

Elicio Therapeutics ($2,756,000)
Elicio's request to GIRF is for a research project that seeks to develop two therapeutic cancer vaccines. Both vaccines have been designed with Elicio's proprietary lymph node-targeting Amphiphile (AMP) platform that "educates" T cells on how to target particular antigens, such as mutated proteins in cancer.

Weill Cornell Medicine ($833,515)
Funding to Dr. Christopher Mason at Weill Cornell Medicine (WCM) will support research utilizing a cutting-edge, sub-cellular spatial profiling technology to reveal novel aspects of colorectal cancer (CRC) heterogeneity and improve our understanding of normal tissues, at both the RNA and protein levels.

Hoosier Cancer Research Network ($1,100,000)
Funding to the Hoosier Cancer Research Network will support the first of its kind clinical trial looking at a novel area of therapy treating cancer called THERA-NOSTICS (therapy + diagnostics). This novel treatment aims to combine therapy with diagnostics in the realm of nuclear medicine and the power of radioisotopes/radiation.

Mayo Clinic ($5,942,244)
This project proposes three different strategies to enhance survival and potentially cure cancer – optimization of the immune system, activation of the immune system to combat cancer, novel combination therapies. Two strategies are in the human clinical trial phase, and one is in the discovery phase.

Rarecyte ($900,000)
Rarecyte has been funded to test gastro-intestinal cancer patient samples within clinical trials to determine circulating tumor cell (CTC) burden and selected biomarker analysis. The emerging trend of personalized medicine ('patient specific therapy') requires deeper understanding of the makeup of CTCs, both at the protein and gene level, to select therapies which will specifically treat the individual patient's cancer.

Weill Cornell Medicine ($290,000)
Liquid biopsies are revolutionizing cancer care. This project focuses on circulating tumor cells (CTCs), where little research has been done to date. Focus on CTCs might allow capture of intact cancer cells that can be used for myriad of biomarker testing that cannot be done on plasma ctDNA. When processed appropriately, they can be noninvasively cultured to develop cell lines and organoids for use in treatment, which now require tissue from a generous biopsy and/or surgery, which isn't always safe or feasible.

University of Iowa ($ 1,698,949)
Colorectal cancer presenting with rare combinations of multiple mutations and demonstrating resistance to standard therapies, requires novel multipronged therapeutic strategies that supersede current conventional approaches. The University of Iowa will test the effect of combining specific drug combinations to target colorectal cancer cells possessing the relevant mutations, delivered in innovative ways.

The University of Texas, MD Anderson ($3,519,021)
With GI Research Foundation support, MD Anderson will conduct three interrelated projects designed to improve survival in patients with BRAF-mutated (BRAFmut) colorectal cancer (CRC), moving promising laboratory findings into new clinical trials to develop novel treatment approaches in the clinic.

Yale University Medicine ($ 1,382,041)
Cancers of the colon, rectum and appendix can spread to the lining of the abdominal cavity and are difficult to detect. Measurement of DNA released by cancer cells is a novel new technology that is being applied to diagnose cancer spread to the lining. However, conventional methods of DNA measurement have low sensitivity to identify this spread. This project, a collaboration with the UChicago Medicine, will harness novel technology developed there (He lab) to detect these cancers early by using exciting novel approaches of liquid biopsy.

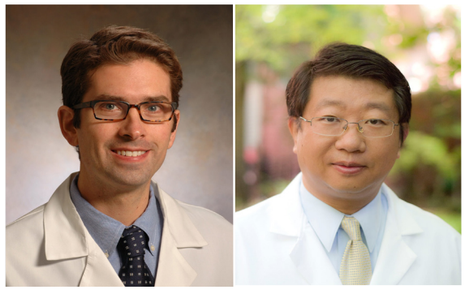
Research 2022

THE PROMISE OF REGENERATIVE MEDICINE

In his acceptance remarks after receiving the Joseph B. Kirsner Award, Dr. Rubin said:

Finally, GIRF has, as they always have, kept their eyes on the bigger picture, and we have worked with them to develop a Regenerative Medicine Program. As mentioned briefly last year during this Ball, regenerative medicine is the study of how tissues develop and mature into different organs, and how tissue injury occurs and changes with age or disease can be repaired or replaced. The potential applications for such a program are incredibly exciting and may include tissue healing in inflammatory bowel disease, organ regeneration in intestinal, liver, or pancreas failure conditions, and ultimately, the discoveries will yield new insights and treatments for GI cancer as well. An institution like the University of Chicago and its multitalented scientists and experts across different departments and specialties is the only place a program like this can be created and succeed, and with GIRF's help, I know we will.

Delivering on that promise, the Foundation began funding regenerative medicine projects like these.

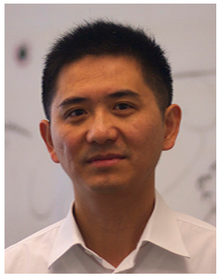


Development of Colorectal Organoid Models to Facilitate Better Patient Care

Christopher Weber, MD, PhD
Le Shen, MB, PhD

The study of organoids – three-dimensional tissue cultures grown relatively inexpensively and quickly from human specimens routinely collected during diagnostic procedures – holds promise in understanding and treating cancer and digestive diseases as organoids can replicate some of the complexity of human organs.

With GI Research Foundation funding, Christopher Weber, MD, PhD, and Le Shen, MB, PhD, aim to answer the question of how often organoids prove predictive of tumor response in colorectal cancer patients. To this end, pathologists, gastroenterologists, and oncologists work together to match drug protocols applied to organoids to standard of care drug protocols administered to patients and then compare the effects of drug protocols on organoids to the effects of the same protocols on patients. This novel study also seeks to optimize and standardize organoid growth approaches and establish a bank and database of colorectal carcinoma organoid lines to support further research.



Early Development of Immunotherapy for IBD

Jun Huang, PhD

The ability to create sustained reduction/elimination of inflammation is key to successful treatment and potentially a cure for patients with IBD.

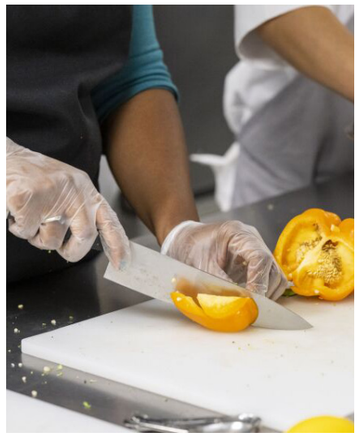
Jun Huang, PhD, and his team at the University of Chicago Pritzker School of Molecular Engineering received support for their research to lay the groundwork for a new immunotherapy for Inflammatory Bowel Diseases (IBD). IBD involves a multi-factor immunological imbalance that drives unhealthy inflammatory response that cause a patient's symptoms.

Researchers have already identified a specific type of immune cell —T-helper type 17 (Th17)— as an important part of the body's immune response in intestinal mucosa. In a healthy patient, Th17 cells are kept in check by regulatory T-cells (Tregs), but in IBD patients, these cells are out of balance, which leads to chronic inflammation. Because existing biologic therapies can lose effectiveness or fail altogether over time, discovering a new immunotherapy using the body's own immune system to correct the imbalance found in IBD could be a gamechanger.

Primarily used today in cancer immunotherapy, chimeric antigen receptor (CAR) T cell therapy uses engineered CARs to target a specific surface protein and trigger specific T cell immune responses. In this study, Jun Huang, PhD, hypothesizes that targeting surface expressed IL-17 on T-helper 17 (Th17) cells, a highly inflammatory cytokine (small proteins important in cell signaling), with a CAR expressed on the surface of regulatory T cells will enable selective, localized production of inhibitory cytokines to suppress the inflammation caused by Th17 cells, thus converting "pro-inflammatory" signals to "anti-inflammatory" responses to eliminate/reduce excessive inflammation in IBD. Because IL-17-mediated inflammation signaling is often observed in the pathogenesis of various autoimmune disorders, such aspsoriasis, leading Dr. Huang to believe targeting it can be beneficial in IBD as well.

Understanding research is a journey anyone can take.

Addressing Community Health & Disparities in Digestive Diseases



With Gene Chang, MD, Ed K. McDonald, MD, IV, and Chef Jeannine Wise lead a GI Research Foundation-supported initative to better understand the role of nutrition and diet in the function of the body's microbiome.

Making a Difference

Cooking Together

With generous support from the GI Research Foundation and others, in 2022, the Digestive Diseases Center established and launched a multifaceted Community Health in Digestive Diseases (CHDD) program. The goal of the program is simple and ambitious: to improve the health of residents on the South Side of Chicago, who are disproportionately affected by chronic disease.

Led by Edwin K. McDonald, MD, IV, Assistant Professor of Medicine at the University of Chicago Digestive Diseases Center and trained chef, along with colleague Jeannine Wise, a chef and partner of world-renowned professional chef Rick Bayless, the CHDD program has established far-reaching roots in the Chicago community.

CHDD has established a curriculum of dietary nutrition and cooking techniques, which are employed in cooking classes for Chicago residents in Englewood, Garfield Park, North Lawndale and many other Chicago neighborhoods. In partnership with the Urban Institute's *Community Champions* program, University of Chicago Pritzker School of Medicine residents also learn these techniques, and apply them with patients, to expand access to healthy cooking and nutrition.

Each class includes a nutrition lecture, cooking instruction, and an *Ask the Doctor* Q&A session. The overall goal of these classes is to help participants learn culinary skills to address health challenges like obesity, colon cancer risk, fatty liver disease, celiac disease, and inflammatory bowel disease. Following each session, participants provide an evaluation and information to further refine the curriculum for the next steps of the Community Health in Digestive Diseases program.

The curriculum is unique, and has been developed with the participants to meet their specific needs and address their specific questions. This curriculum focuses on key components of kitchen health and culinary methods, as well as anatomy and physiology.

For culinary methods, the curriculum includes: kitchen safety and sanitation; knife skills; roasting, braising, sautéing, and steaming as alternatives to frying; soup fundamentals; salad and vinaigrettes; and healthy baking.

The health awareness curriculum covers basic anatomy; the fundamentals of absorption and digestion; how to read a food label; diet and cancer; sodium and high blood pressure; diet and diabetes; gut health and the microbiome; healthy breakfast; and macronutrients.

In the next phase of the program, Dr. McDonald and Chef Jeannine will work with Eugene B. Chang, MD, Martin Boyer Professor of Medicine at the University of Chicago Digestive Diseases Center, to examine the effectiveness of a food and nutrition intervention on the composition of individual patients' microbiome. This new information will help physicians understand the specific impact that diet and nutrition have on the microbiome, and help establish the role that educational interventions play in supporting digestive health.

Stories about this important work has been featured in both the Chicago Tribune and the Chicago Sun-Times. Contact info@girf.org for more information.

Research 2022

Through a competitive grant application process, the GI Research Foundation funded the following novel investigator initiated research programs in 2022.

Characterizing the effects of ulcerative colitis on rectal structure, function and symptomatology using novel imaging modalities.

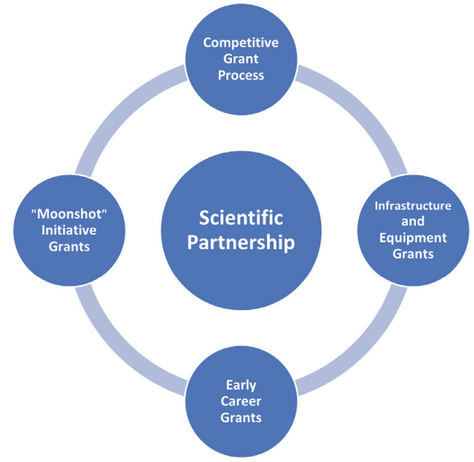
Noa Krugliak Cleveland, MD

Even with resolution of bowel inflammation, many ulcerative colitis patients continue to experience disease symptoms related to stool frequency and urgency. Conversely, absent such symptoms, some patients show bowel inflammation during endoscopy or in histological examination. This study aims to explore what disease factors contribute to persistent bowel discomfort in patients, hypothesizing that structural and functional changes to the rectum resulting from chronic inflammation, rather than active inflammation itself, cause certain symptoms. Additionally, study investigators seek to expand how clinical tools such as MRI, surgical colectomy, and intestinal ultrasound can detect and monitor disease changes over time and evaluate the reversibility of these changes.

Host and microbial predictors of ileal pouch inflammation in ulcerative colitis patients

Sushila R. Dalal, MD

J-pouch patients present a unique population to study the development of new inflammation in inflammatory bowel disease. In these patients, the J pouch, acts as a “new rectum”, and often appears normal. However, about 40% of patients develop inflammation in the J-pouch, called pouchitis, over the first two years. When pouchitis doesn’t respond to initial treatment, patients sometimes develop either chronic inflammation or Crohn’s disease-like inflammation in the pouch, requiring them to resume immunosuppressive medications, or require removal of the pouch altogether. However, there currently is no good way to predict who will have a good quality of life with a J pouch and who will develop this inflammation. This study will look at the small intestine immune and microbial metabolite profile at the time of the surgery, in order to determine whether a certain host immune profile or pattern of microbial metabolites can predict J pouch outcomes. This information could yield a way to help make better decisions for patients at the time of surgery.



Roles of microbiota-derived metabolites in colon cancer development

Yan Chun Li, PhD

A high-fat, low-fiber Western diet has long been considered a risk factor for the development of colon cancer. This has been attributed to the disruption of the gut microbiota, and the production of short chain fatty acids in the gut, some of which has been thought to be protective against cancer development. However, the presence of one of these short chain fatty acids, acetate, and associated metabolic enzyme Acss2, may encourage the development of neoplastic (cancer) cells in the colon. Parsing these factors will help elucidate how dietary/nutritional factors and gut bacteria interplay to influence colon cancer development, which in turn may help identify new therapeutic targets (such as Acss2) for colorectal cancer treatment.

Exploring the neurophysiology of central nervous system involvement in pediatric celiac disease and “brain fog.”

Rachel Lieberman, Ritu Verma MBBS, Bana Jabri MD, PhD, Martina Williams, MD, MPH, & Julia Kleinhenz, MD

Though anecdotal observation points to a connection between celiac disease and “brain fog,” a cognitive/mood impairment typified by difficulties such as depression and diminished mental acuity, scientists lack the data necessary to explain brain fog as a symptom of celiac disease and to evaluate the impact of a gluten-free diet (the only known treatment for celiac disease) on brain fog. This study follows children newly diagnosed with celiac disease prior to and throughout the first year of their adherence to a gluten-free diet, assessing neurological manifestations of their disease via bloodwork, functional brain MRI, EEG, and psychological testing. In gathering measurable information about brain fog, correlating brain fog symptoms with celiac antibody levels, and tracking brain fog symptoms on and off a gluten-free diet, study investigators seek to clarify the specific mechanisms of gut-brain interaction in pediatric celiac disease and its treatment.

Research 2022

Through a competitive grant application process, the GI Research Foundation funded the following investigator initiated research programs in 2022.

Reprogramming stem cells to treat inflammatory bowel disease
Cambrian Y. Liu, MD

Myriad medical therapies and surgical treatments treat the inflammation caused by inflammatory bowel disease, but even with effective treatment, for many patients, the underlying disease chronically returns. This study proposes to examine the role that deficient stem cells may play in the chronicity of IBD, and investigate whether “defective” stem cells may serve as an underlying mechanism in the disease state. Novel methods for stem cell research, including three-dimensional modeling of diseased tissue, imaging, lineage tracing, IBD mouse models, stem-cell biology, and bioinformatics and study design that capitalizes on the potential of regenerative medicine could hold the key to unlocking the promise of stem cell treatment for IBD.

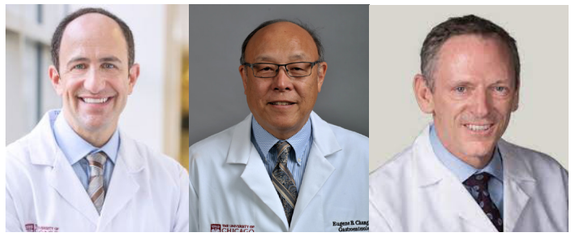
The role of bile acids in colorectal cancer disparities
Sonia S. Kupfer, MD

African Americans are among the highest risk for colorectal cancer development, but the specific reasons African Americans develop this disease at higher rates than other groups remain unknown. This study will investigate the role that bile acids may play in this disparity, and utilize organoid technology and other cutting-edge techniques to study these population differences. This innovative study has high impact potential: to clarify the interrelated roles of diet, microbiome and host responses in colorectal cancer disparities. This discovery could translate into future intervention trials and new disease markers that ultimately will reduce cancer disparities.

New diagnostic and therapeutic strategies for perianal Crohn’s disease
Benjamin McDonald, MD, PhD

Perianal Crohn’s disease is a particularly aggressive form of Crohn’s disease encompassing perianal fistulas, perianal abscesses, anal fissures, and anal strictures . It affects approximately 25% of CD patients and is associated with a more aggressive disease course, a need for more surgical intervention, and significant negative impact on patient quality of life. Once perianal disease develops, current medical and surgical therapies are unable to reverse tissue damage, which leads to worse disease outcomes for patients. This study investigates the use of perianal ultrasound to detect perianal disease before it creates clinical symptoms, and also looks at inflammatory pathways for perianal disease in order to identify new, superior, treatment strategies.

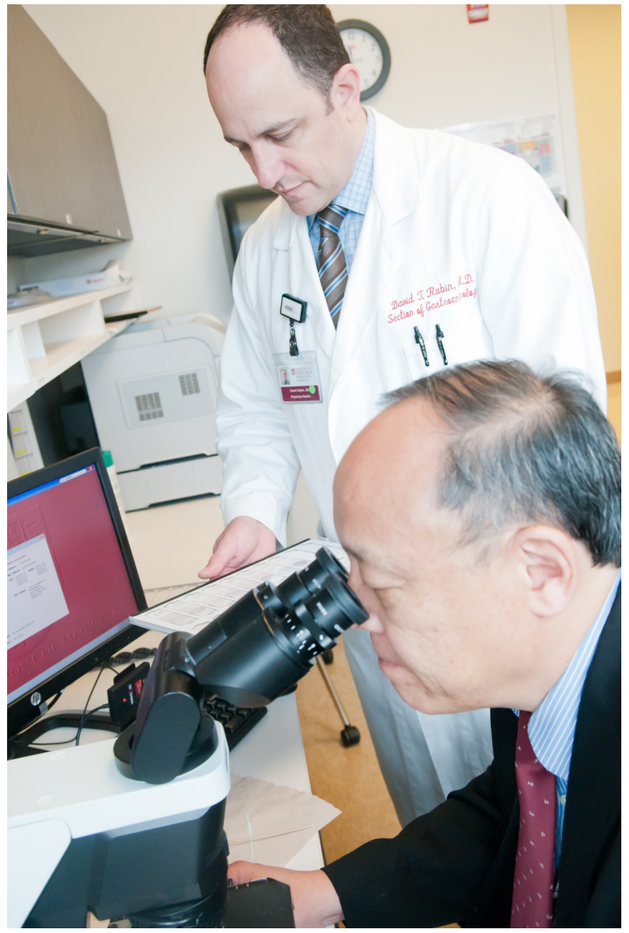
CRITICAL SUPPORT OF INFRASTRUCTURE

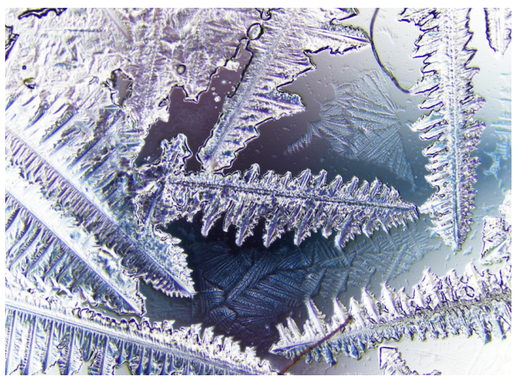


GI Research Foundation Translational Core Registry
David Rubin, MD, Eugene Chang, MD, and Michael Charlton, MD

Through GIRF’s ongoing investment, the University of Chicago Digestive Disease Center maintains a large registry of over 35,000 biospecimens drawn from over 10,000 patients seen at the University of Chicago subspecialty clinics for IBD, liver disease, pancreatic disease, esophageal disorders, hereditary GI cancers, celiac disease, liver tumors, and obesity. Given the breadth of patient phenotypes, clinic data, and biospecimens available, this translational core database and biosample repository is widely utilized by investigators at the University of Chicago and beyond. Funding support for the research and clinical staff needed to run this registry, and ensures that this resource will continue to be utilized by physician scientists to produce high-quality research studies.

The Translational Core Registry is unique to the University of Chicago Digestive Diseases Center, and critical infrastructure for scientific inquiry, as it is a means of optimizing data collection not just for one study, but for many, and helps to faciitate interdisciplinary research across otherwise siloed areas of expertise.





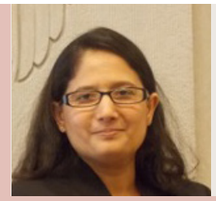
Research 2022

Each year, the GIRF Associates Board awards early career grants to young investigators, providing a springboard at a critical time in an investigator's scientific career. These were the recipients of the 2022 awards.

Early Career Award

Ankit Malik, PhD, Research Scientist

Title: Role of antigen presentation by intestinal epithelial cells in T-cell immunity
Mentor: Bana Jabri, MD, PhD
Type of Research: Basic/Translational
Research Focus: The sensing of IFN-γ during colitis promotes the presentation of self and microbial antigens by the intestinal epithelial cells (IECs), that in turn mediate protective T cell (immune) responses.
Study subject: Animal (mouse)
Impact: Understanding the aberrant immune response to microbes living in the gut and deriving nutrition from their host is key to understanding the development of colitis. The epithelial tissue, or the thin layer of tissue that lines the intestinal tract, plays a role in this interaction. These studies will shed light on the nature of antigens presented by the intestinal epithelial cells, and the function of epithelial IFN-γR, a specific signaling cascade. The studies use MHCI and MHCII mice genetically developed to help isolate these characteristics in colits, and will provide important insights into our understanding of how IECs regulate mucosal immunity and inflammation.



Early Career Award

Shabana M. Shaik, PhD, Research Scientist

Title: Characterization of serum metabolites in Alzheimer's mice models with an antibiotic-altered gut microbiome
Mentor: Sam Sisodia, PhD, Dept. of Neurobiology
Type of Research: Basic/Translational
Research Focus: Alterations in gut microbiome can influence integrity of blood-brain barrier and promote transfer of immunomodulatory metabolites through circulation to CNS to effect neuroimmune functions.
Study subject: Animal (mouse)
Impact: Neuroinflammation plays a part in the development of Alzheimer's disease and other forms of dementia. There are also observed sex differences in both the incidence rates of Crohn's disease and ulcerative colitis, as well as the Alzheimer's disease in IBD patients. This study helps to elucidate the ways that microglia, or immune cells in the brain, are impacted by differences metabolism of and metabolites created by the gut microbiome, and that pathways that connect the gut and the brain.

Early Career Award

Zhenrun J. Zhang, PhD, Postdoctoral Scholar

Title: Impact of lantibiotics on human gut commensals
Mentor: Eric G. Pamer, PhD
Research Focus: Putative lantibiotic resistance systems (LRS) among human gut commensals (gut microbiome) contribute to the gut commensals' resistance against gut- and food-derived lantibiotics. These dynamics are important in better understanding how to prevent drug resistant intestinal infections.
Study subject: Human gut microbes
Type of Research: Basic/Translational
Impact: Interbacterial defense systems among human gut commensals (bacteria which receive nutrition from the host) are important in mediating resistance to lantibiotics (a kind of antibiotic well known in the production of dairy products, such as cheese). Understanding the structure-activity relationship of lantibiotics, and ecological implications of lantibiotic resistance systems in human gut microbiome in vivo, and better understanding these relationships can help guide development of novel therapeutics against enteric bacterial infections in future work.

Special Events

2022 GI Research Foundation Annual Ball

The premiere fundraising event of the GI Research Foundation raised over $1.3 million dollars for GI research in 2022.

Karyn Hurwich and Kathy Shafer, Ball Co-Chairs

On Saturday, June 4, 2022, the GI Research Foundation Annual Ball celebrated the courageous patients and devoted physician-scientists fighting to prevent, treat, and cure digestive diseases. Held at The Geraghty, a chic event space in Pilsen, the event marked the triumphant return to an in-person gala experience, and was a smashing success – raising $1.3+ million for research at the University of Chicago Medicine Digestive Diseases Center.

David T. Rubin, MD

recipient of the Joseph B. Kirsner award, with Howard Grill

Ira Hanan, MD

recipient of the 2022 Lifetime Achievement award, with Andrew Arohnson, MD

2022 Associates Board Cocktail Party

On Friday, September 23, 2022, the GI Research Foundation Associates Board and supporters came together at the Associates Board Annual Cocktail Party: *[Re]United for GI Health*.

Held at the Radisson Blu Aqua hotel in downtown Chicago, the cocktail party was the group's first celebration and fundraising event since the beginning of the Covid-19 pandemic.

Jordan Hirsch, Associates Board President, thanked the energetic crowd and emphasized the importance of the evening, explaining, "We simply cannot fulfill our mission of advancing the science, medicine, and treatment of gastro-intestinal diseases at the University of Chicago Digestive Disease Center without your support. Thank you for meeting the moment with your generosity."

The evening raised tens of thousands of dollars, funds which will support the Board's annual grant competition for early career physician-scientists in Spring 2023. Event sponsors included corporate sponsors Home Infusion Options and Janssen; as well as the Huiras, Turban, and Grill families.

As the youngest Associates Board President in the organization's history, Jordan Hirsch, saw the evening as a smashing success. "Just looking at this room tonight, it feels awesome to say we are here, together, and doing what the Associates Board does—raising money, and giving it away to researchers."

2022 Associates Board Cocktail Party

2022 All Stars

Monday, August 29th, the GI Research Foundation hosted the Larry A. Pogofsky All-Star Challenge—On the Greens at the Bryn Mawr Country Club in Lincolnwood. Pro-athletes – including Chicago greats Ozzie Guillen, Chris Chelios, Willie Gault and more – joined foursomes to honor Larry's love of sports and continue his legacy of funding research to better treat, prevent and cure digestive diseases.

Golfers enjoyed breakfast, contests, a barbeque lunch along the course, and golf until the skies turned dark. The rain didn't dampen the high spirits. Guests moved indoors for a 19th Hole Reception cocktails donated by 8 Hospitality, Tito's Handmade Vodka and El Bandito Tequila; silent and live auction packages from Bergie's Sports Card Dugout, Chicago White Sox, Milwaukee Bucks, Rich Harvest Farms and more; and music from Gold Coast Events. Thanks to generous sponsors and donors– including Birdie Sponsors Belmont Bank & Trust and Jeff & Kelly Brincat– the All-Star Challenge raised more than $174,000 for digestive diseases research.

Larry A. Pogofsky was a die-hard baseball fan who was also passionate about healthcare research thanks to a life-changing experience at the University of Chicago Medicine Digestive Diseases Center.

PATIENT ALL-STAR

SHELLY MILLER

In 1995, at age 40, Shelly Miller had had rough six months and a series of health setbacks, including an arterial blockage, diabetes, and intestinal bleeding. The bleeding quickly led to her diagnosis of Crohn's disease, and Miller began treatment. When infliximab (Remicade) became provisionally approved for the treatment of Crohn's disease, Miller was one of the first people to receive it for treatment, and her case helped determine dosing intervals for future patients.

Miller had a demanding job as Vice President of Sales and Marketing for an auto parts distributor in Philadelphia. A career move later, Miller found herself in Chicago, in the care of the University of Chicago IBD Center team. Given the severity of her case, her family history of colon cancer, and the medical therapy available at the time, her best treatment option became surgery to remove her colon. When her IBD team recommended ileostomy surgery, Jan Colwell, APN, CWON, head of the Ostomy Care Clinic, stepped in.

"Jan is just amazing.... I really credit her for the fact that I'm still alive. I really truly do... She was such an amazing advocate for me when things were really, really bad. We became closer through it, and we're very good friends now. She's just an amazing person," says Miller.

Colwell and the IBD team at the University of Chicago helped Miller transition to life with an ileostomy. While her first surgery, performed by senior colorectal surgeon Roger Hurst, was successful, subsequent complications from gastric sleeve, hernia, and reconstructive surgery necessitated additional treatment to correct stoma irregularities.

"[Post-surgery] A few years went by and I was struggling." explains Miller. "Jan [Colwell], God love her, she just kept sticking with me and advocating for me. She went back and she said, 'We cannot leave this 50-something year old woman, in the prime of her life, and her career, in a place where she can't work again, and she can't live her life.'"

Following corrective surgery for Miller's stoma, she was able to make a full recovery without further complications.

Now retired and residing near sunny Palm Springs, Miller now serves as the Secretary of Friends of Ostomates Worldwide (FOW-USA), an organization which helps to collect and distribute ostomy supplies internationally to patients who need them. For the past 12 years, Miller has served as a Board Member, newsletter editor, Public Relations Chair, and Vice President of FOW-USA.

"It's important for me to give back wherever I can. It's enormously gratifying," says Miller.

Financial Overview 2022

STATEMENT OF ACTIVITIES
Year Ended June 30, 2022

REVENUE AND SUPPORT

Fundraising - special events	$1,508,206
Donations - unrestricted	$211,760
Bequests - unrestricted	$579,760
Interest and dividend income	$65,635
Realized loss on investments	$(1,092)
Unrealized loss on investments	$(117,319)
TOTAL REVENUES AND SUPPORT	**$2,246,950**

EXPENSES

PROGRAMS AND SERVICES	
Grant awards	$1,525,364
Salaries and benefits	$210,028
Venues for educational programming	$86,673
Newsletter and education	$25,587
Program office expenses	$14,855
Travel and meetings	$4,958
PROGRAMS AND SERVICES TOTAL	**$1,867,465**
GENERAL AND ADMINISTRATION	
Salaries and benefits	$70,010
Professional fees	$12,804
Rent and office expenses	$7,353
Meetings	$1,486
GENERAL AND ADMINISTRATION TOTAL	**$91,653**
FUNDRAISING	
Fundraising event expenses	$269,108
Salaries and benefits	$70,010
Donation processing fees	$20,057
Postage and office expenses	$4,951
FUNDRAISING TOTAL	**$364,126**
TOTAL EXPENSES	**$2,323,244**
CHANGE IN NET ASSETS	**$(76,294)**
NET ASSETS, BEGINNING	**$4,240,989**
NET ASSETS, ENDING	**$4,164,695**

For over 60 years, our research investments have contributed to a greater understanding of digestive disease and its treatment options, thanks to the generous support of our donors. We take seriously our responsibility to the digestive disease community, and we work hard to maximize every dollar given to our mission.

Howard Grill, GI Research Foundation Board Member and Vice President Finance/Treasurer

80%

of your support goes directly to research grants and educational programs

Auditors: Anna Nalls, CPA
The assets within the GastroIntestinal Research Foundation are managed accordance with written policies formally approved by the Board of Directors. The Finance Committee works with professional investment managers to monitor the performance of these investments against appropriate market indices. The financial statements summarized above have been audited by Anna Nalls, CPA. The complete audited financialstatements and copies of our 990 are available upon request by contacting the Foundation office or by visiting https:/ giresearchfoundation.org/.

STATEMENT OF FINANCIAL POSITION
Year Ended June 30, 2022

ASSETS

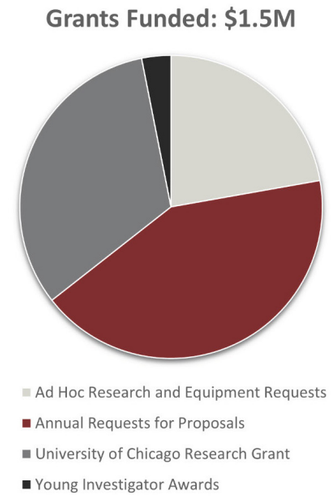
CURRENT ASSETS	
Cash and cash equivalents	$873,953
Investments	$2,946,319
Accounts receivable	$338,463
Prepaid expenses	$24,000
Total current assets	$4,182,735
TOTAL ASSETS	**$4,182,735**

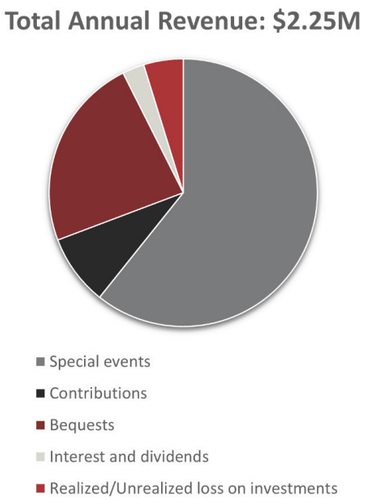
LIABILITIES AND NET ASSETS

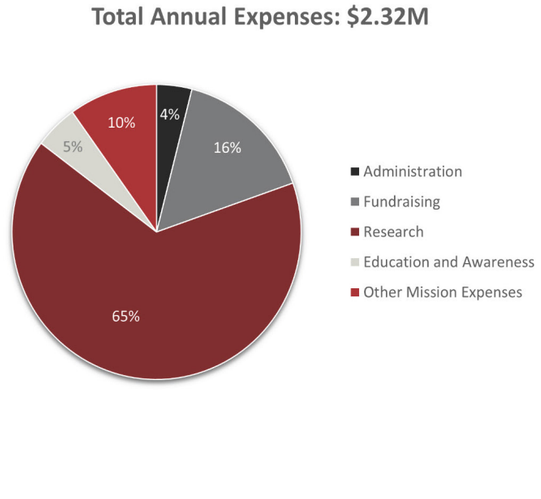
CURRENT LIABILITIES	
Accounts payable	$9,643
Accrued expenses	$8,397
TOTAL LIABILITIES	**$18,040**
NET ASSETS	
Without donor restrictions	$4,164,695
With donor restrictions	
TOTAL NET ASSETS	**$4,164,695**
TOTAL LIABILITIES AND NET ASSETS	**$4,182,735**

$1.5M

invested in funded digestive diseass research







Board Leadership 2022

2022 **BOARD OF DIRECTORS**

OFFICERS
Yekaterina Chudnovsky – President (outgoing); Chairperson (incoming)
Kathryn Karmin Shafer – Executive Vice President (outgoing); President (incoming)
Howard A. Grill – Vice President of Finance and Treasurer
Mark de Souza – Vice President of Fundraising and Development
Biana Lanson, MD – Vice President of Fundraising and Development (outgoing); Vice President of Grantmaking (incoming)
Mark A. Waldeck – Vice President of Marketing and Communications
Benjamin Pogofsky – Vice President of Board Development
Brad Peterson – Secretary (incoming)

DIRECTORS
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Scott Attar
Eric Berlin
Michael P. Cogan
Russell D. Cohen, MD
Steven R. Davidson
Jeffrey A. Fine
Peter D. Goldman
Heidi Henderson
Jordan Hirsch (*ex officio*)
Karyn Hurwich
Matthew Lebenson
Jonathan Merel
Benjamin Riback
Seymour Taxman

2022 **SCIENTIFIC ADVISORS**

David T. Rubin, MD, Joseph B. Kirsner Professor of Medicine; Section Chief, Gastroenterology, Hepatology and Nutrition, The University of Chicago Medicine
Eugene B. Chang, MD, Martin Boyer Professor of Medicine; Director, Inflammatory Bowel Disease Research Center in the Biological Sciences Division, The University of Chicago Medicine
Michael R. Charlton, MBBS, Professor of Medicine; Director, Center for Liver Diseases; Co-Director, Transplant Institute, The University of Chicago Medicine

2022 **ADVISORY COUNCIL**

Ronald Borden, Ronald J. Borden & Company, Ltd
Amy Tara Koch, Author and Journalist
Ralph Kaufmann, *deceased*
Erica Matagrano, Amgen
Kelly O'Connor, StageLight Group
B.H. Gerald Rogers, MD, The University of Chicago Medicine
Aaron Rosdal, Prologis
David A. Rubin
Saul Rudo, Katten Muchin Rosenman LLP
Spencer G. Sachs, SCG Asset Management
Gary Singer, Kobre & Kim
Hilary Wolfe, Northern Trust

Board Leadership and Staff 2022

2022 **ASSOCIATES BOARD**

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Jordan Hirsch – President
Sushila Dalal, MD – Medical Advisor, Assistant Professor of Medicine, Section of Gastroenterology, Hepatology & Nutrition, University of Chicago Medicine
Ashley Sidebottom, PhD – Scientific Advisor, Platform Director, Host-Microbe Metabolomics, University of Chicago Duchossois Family Institute

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Logan Turban
Katherine Waldeck
Morgan Waldeck

2022 **STAFF**

Jackie Casey, JD, Executive Director
Deborah Barnard, Director of Major Gifts
Allison Thielen, Finance and Operations Manager
Brittany Zelwin, Development Manager

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GIRF.org

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