THE DIGESTIVE HEALTH FOUNDATION

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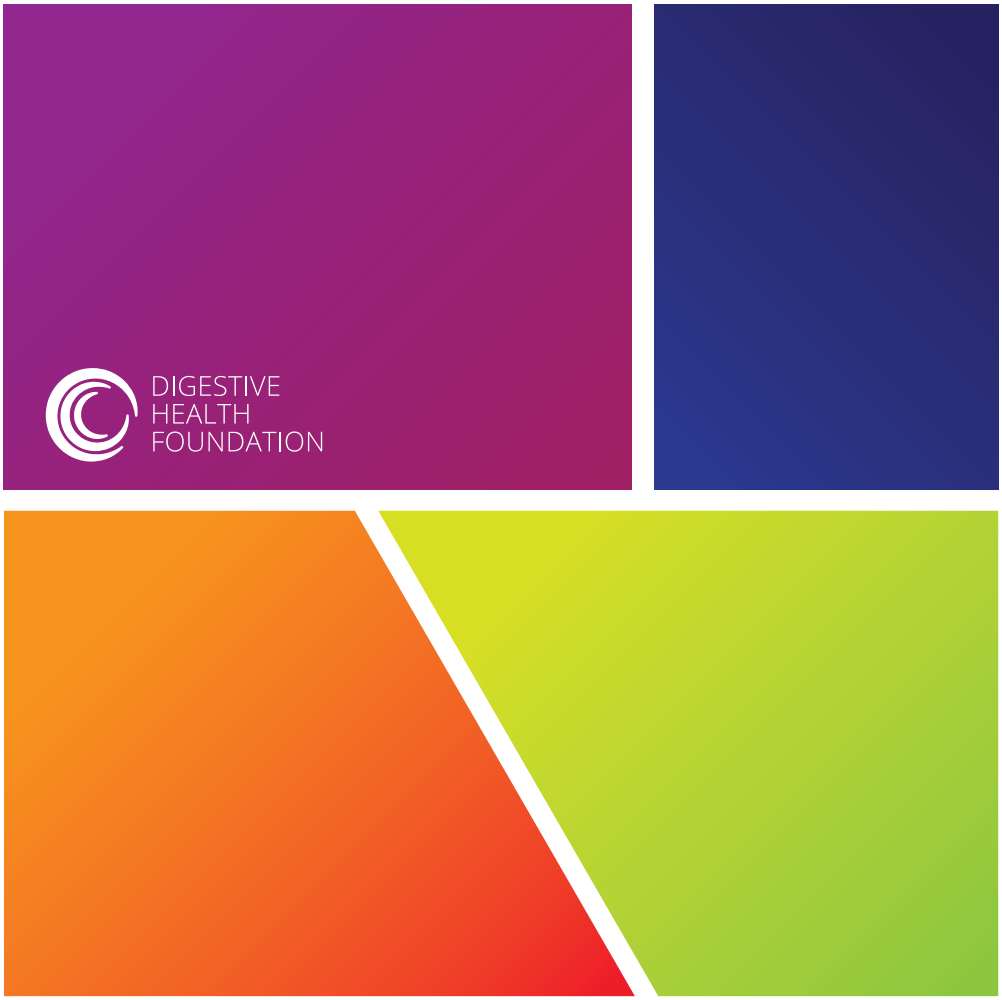


TOGETHER ON THE TERRACE

DONOR APPRECIATION & GRANT AWARDEES

PRESIDENT'S LETTER

Dear Friends and Family,

While it may have felt like the world stopped during the pandemic, gastrointestinal diseases unfortunately did not. Digestive diseases continue to adversely affect an estimated 60-70 million Americans every year, costing more than $142 million. But just as we are all hopeful for a promising return to normal, the DHF has renewed hope for the future of digestive health.

Although 2020 was a difficult year, the DHF remained committed to raising funds to support cutting-edge medical research, physician training and education at the renowned Northwestern Medicine Digestive Health Center. Our support helps doctors and scientists prevent, treat and ultimately cure a spectrum of digestive disorders including colon, pancreatic and esophageal cancers; Crohn's and Celiac disease; Hepatitis and other liver diseases; ulcerative colitis; and swallowing disorders.

Since our inception six years ago, the DHF has funded 67 crucial annual grants as well as ongoing research studies including the DHF Biorepository, a blood and tissue bank used for digestive disease research that is one of the few databases of its kind in the world. We also helped fund a Center for Artificial Intelligence (AI) which has since spurred three different patents, the most promising of which is the use of heat maps to diagnose diseases.

Most recently, our 2021 grants program was able to fund 13 brand new research initiatives aimed at the diagnosis and treatment of a wide array of GI health issues including: Inflammatory Bowel Disease (IBD), colorectal cancer; Gastroesophageal Reflux Disease (GERD); Autoimmune Hepatitis; Colitis; liver transplants; pancreatitis; newborn liver failure; and pediatric Eosinophilic Esophagitis (EoE).

In addition to the promising research, the Ambassador Board's "Together on the Terrace" event at the MCA on June 5 marked the first in-person gathering for the DHF since the pandemic began. We're excited about the energy the newly formed Ambassador Board brings to the DHF and we welcome their ideas and initiatives going forward.

We realize none of this would be possible without your continued support. Thank you for providing those living with digestive illness with hope for a bright future.

Lee Gould,

President, DHF Board of Directors

AB PRESIDENT'S LETTER

Dear Friends,

On behalf of the Digestive Health Foundation Ambassador Board, I would like to thank you for supporting our "Together on the Terrace" event at the MCA. After more than a year apart, it was exciting to see so many friends of the DHF come together (either in-person or virtually) in support of a very important cause.

As you may know, the DHF Ambassador Board is a passionate, energized team of patients, providers and family members that understand the daily struggles of living with digestive illness. I myself have been fighting Crohn's disease for many years and know all too well how debilitating living with a chronic illness can be. But, thanks to the ongoing research and committed physicians at the Northwestern Medicine Digestive Health Center, I have been able to live a full and happy life. Many Ambassador Board members can share similar stories of hope and healing, which is why we remain committed to raising funds to help accelerate groundbreaking medical discoveries – discoveries that have the power to transform digestive disease into digestive health.

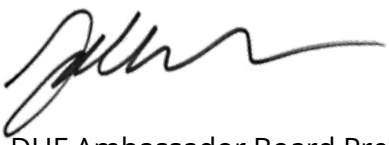
In addition to supporting the crucial work of the Northwestern Medicine Digestive Health Center, the DHF Ambassador Board also aims to promote greater equity in access to medical care and education. To that end, proceeds from our Together on the Terrace event will benefit many exciting programs such as the **DHF MCAT Prep Program** and the **Elizabeth Blackwell Fund**.

Created in 2020 in partnership with the I Am Abel Foundation, the **DHF MCAT Prep Program** provides much needed infrastructure for under-represented students in their efforts to enter medical school. DHF provides test prep funding, resources and mentoring. Our goal is to expand and continually grow the program in volume and reach to include more I Am Abel students each year.

With the **Elizabeth Blackwell Fund**, DHF supports gender equity in research by honoring the first woman to earn a medical degree in the United States. This grant provides support to female researchers as they work toward independent funding while balancing work and family. Taking chances is an essential component of developing a career as a research scientist and these funds provide support for creativity.

We greatly appreciate your support of the DHF and the goals of our newly formed Ambassador Board. Thank you for giving those of us living with digestive illness the gift of hope.

Jason Press



DHF Ambassador Board President

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Your dedication to your patients
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Very special thanks to
Dr. Stephen Hanauer
for the amazing care and commitment
he has shown our family.

The Saltoun Braun Family

We proudly support

the Digestive Health Foundation and the newly formed DHF Ambassadors' Board, as it continues to strengthen its mission to transform digestive disease into digestive health. Special thank you to Dr. John Pandolfino, Dr. Stephen Hanauer, Dr. Scott Strong, Dr. Michael Ruchim, the physicians of the Digestive Health Center, and the DHF Board members and the DHF Ambassadors' Board members for their tireless efforts to ensure success of this year's exciting events.

Stephanie & Michael Baum

THANK YOU!

Thank you to every Digestive Health Foundation patron for your generous contributions and commitment to our events, our research and our DHF Family.

Lee Gould
President of DHF

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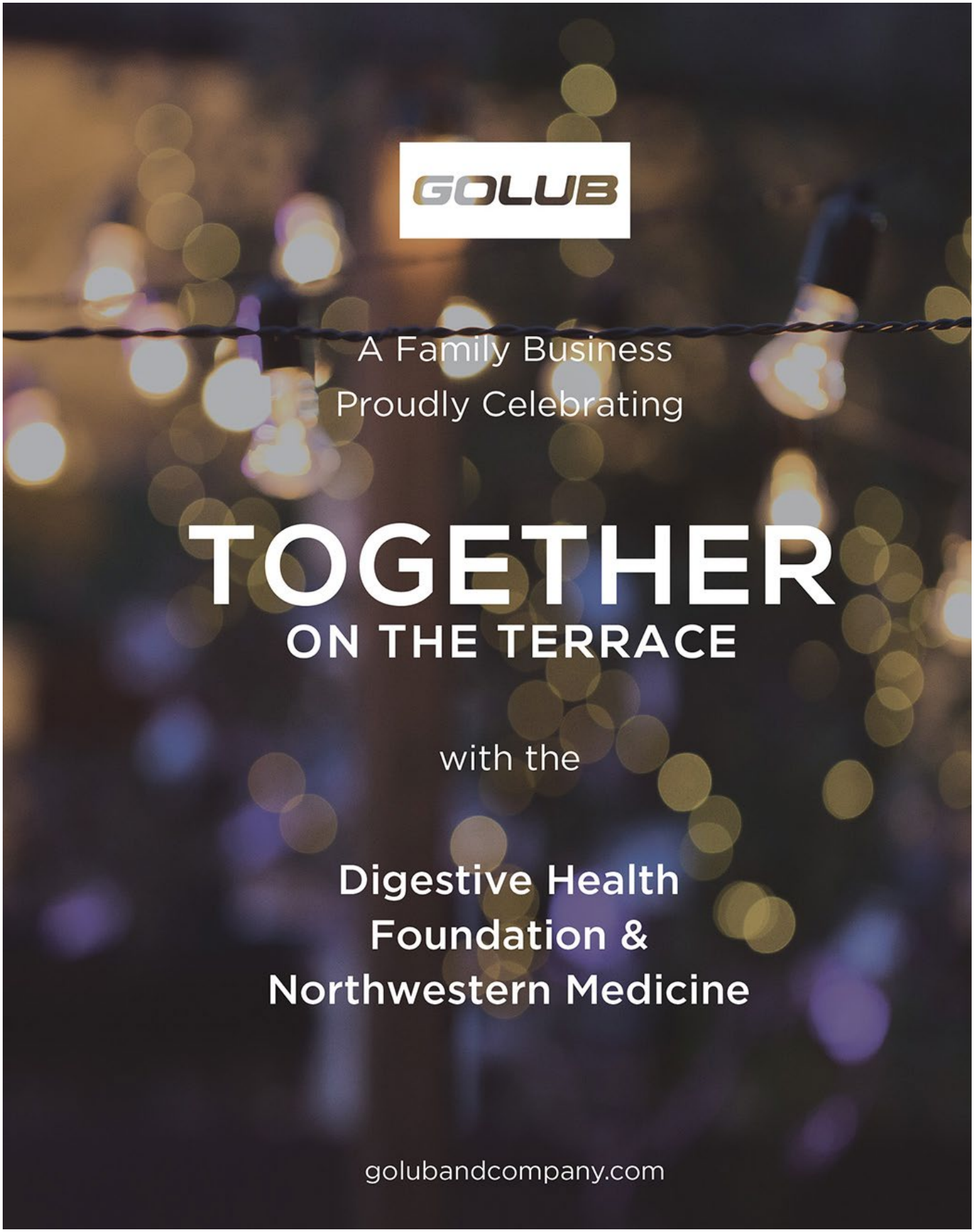
Special thank you to
Dr. John Pandolfino, Dr. Stephen Hanauer,
Dr. Scott Strong, Dr. Michael Ruchim,
the physicians of the Digestive Health Center,
and the DHF Board members
and the DHF Ambassadors' Board members
for their tireless efforts to ensure success
of this year's exciting events.

Erica and Michael Fishman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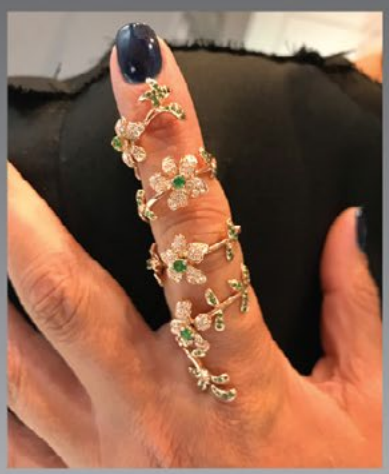

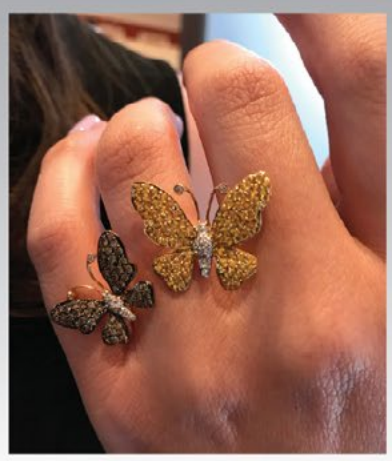

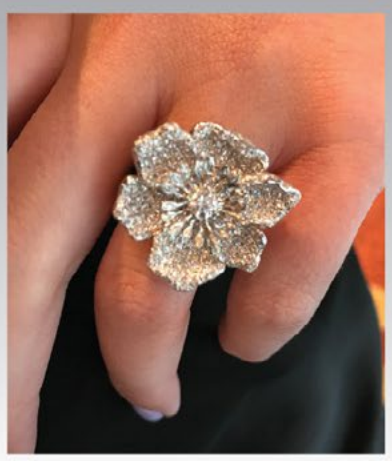


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CONGRATULATIONS TO OUR NEWEST GRANT AWARDEES

Improving Diagnosis and Outcomes in Newborn Liver Failure

Principal Investigator: Sarah Taylor, MD

Gestational alloimmune liver disease (GALD) is the leading cause of liver failure in newborns. The rare disease occurs when maternal antibodies injure the developing liver of the fetus during pregnancy. Infants with GALD require prompt diagnosis and treatment at birth. Yet, even with treatment, about 50 percent of infants die from GALD. Quickly obtaining a precise and reliable diagnosis remains challenging. Clinicians lack accepted criteria based on histology findings, and no biomarkers specific for GALD exist. To overcome these gaps in clinical care, Dr. Taylor's lab will create histologic scoring criteria that can be easily disseminated to enable prompt and reliable diagnosis of GALD. Evaluating the RNA of livers from affected patients, the Taylor team hopes to identify new blood tests that will differentiate GALD from other causes of neonatal liver failure. Better understanding the disease process of GALD will help to launch future research and the development of live-saving therapies for these young patients.

Genetic Analysis of Gut Immune Cells Conferring Resistance to Anti-TNFα Therapy in IBD

Principal Investigator: Ronen Sumagin, PhD

Individuals with inflammatory bowel disease (IBD) require timely and effective therapies. When conventional medications such as corticosteroids or 5-aminosalicylates fail to work, biologics that block a critical inflammatory molecule called tumor-necrosis-factor alpha (TNFα) are commonly prescribed. Several biologics targeting TNFα include infliximab, adalimumab, etanercept and certolizumab pegol. Unfortunately, these drugs offer no relief to one third of patients. In previous work, the Sumagin lab and others established the role of immune cells called neutrophils in IBD. More recent studies revealed that in inflamed tissue there are diverse neutrophil populations with distinct functions. Dr. Sumagin plans to use innovative single-cell sequencing to map neutrophil diversity in IBD. His team will look to determine whether specific neutrophil subtype(s) dictate resistance to anti-TNFα therapy. This high-risk, high-reward effort offers great promise for unraveling new disease processes and identifying predictive biomarkers of treatment outcomes or drug targets to prevent anti-TNFα resistance in patients with IBD.

Develop and Assess the Distensibility and Pressurization in Esophageal Body and the Lower Sphincter during Bolus Transit, Using 4D Manometry Analysis of High-Resolution-Impedance-Manometry (HRIM) Measurements

Principal Investigator: Wenjun Kou, PhD

High-resolution impedance manometry (HRIM) aids in diagnosing esophageal motility disorders. It works by measuring pressures and fluid movement in the esophagus and lower esophageal sphincter. The Kou team plans to transform an HRIM-based analysis technique into new analytical tools with specific metrics/outcomes for use in clinical practice. Taking HRIM analytics a step further offers great value for better evaluating esophageal function. The metrics to be studied include bolus retention; intrabolus pressure (IBP) and distensiblity of the esophageal body at each phase; pressure and distensiblity of esophagogastric junction (EGJ) as well as emptying flow rate. The study will involve 1) designing and implementing algorithms on metrics calculation and 2) deriving a metrics dataset from HRIM studies of various phenotypes. The team will then use statistical analysis and machine learning to evaluate the discriminating power of the metrics and derive classification models. Dr. Kou will conduct a further comparison with similar outcomes from panometry—another tool used in esophageal evaluations.

Is a Simple Measure of Nervous System Activity (Heart Rate Variability) Related to Fatigue in IBD and Is It a Possible Treatment Target?

Principal Investigator: Tiffany Taft, PsyD, MIS

Fatigue remains a major issue in the treatment of inflammatory bowel disease (IBD). Many patients find it just as concerning as abdominal pain or bowel control. Lacking reliable therapeutic options, clinicians grapple with how to adequately manage it. Dr. Taft believes heart rate variability (HRV)—the change in time intervals between each heartbeat—may play a role. The Taft team plans to study the relationship between normal HRV changes and fatigue in patients with IBD, while taking into account the influence of other factors such as inflammation, mood and sleep. The investigators will measure markers of inflammation as well as common vitamin and mineral deficiencies in IBD patients via a phlebotomist blood draw at the start of the study. Participants will wear Fitbit devices to monitor their HRV continuously over two weeks. If a relationship exists between low HRV and fatigue, improving HRV via behavioral techniques such as slow-breathing and other relaxation methods has the potential to greatly improve patient outcomes and quality of life.

Using a Novel Imaging Method of the Heart and Liver to Define which Patients with Cirrhosis Are at Risk for Heart Failure before and after a TIPS Procedure (a Procedure for the Treatment of High Pressure in the Vein that Carries Blood from the Digestive Organs to the Liver)

Principal Investigator: Lisa B. VanWagner MD, MS

Cirrhosis of the liver affects millions of Americans and leads to increased and life-threatening pressure in the blood vessels of the liver. One of the core treatments for this potentially deadly complication is a procedure called "TIPS." While effectively reducing pressure in the liver, TIPS can result in heart failure in at least 20 percent of patients. The ability to identify patients at risk for cardiac dysfunction would allow clinicians to put into place targeted prevention strategies before and after TIPS. With that aim in mind, the VanWagner team will be evaluating new imaging methods of the heart and liver to better understand how TIPS alters liver hemodynamics and changes cardiovascular structure, function and flow in patients with cirrhosis undergoing TIPS. Study findings could lead to interventions to prevent the development of heart failure in this at-risk patient population.

Exploring the Relationship between Changes in Blood Sugar throughout the Day and Symptom Severity in Patients with IBD

Principal Investigator: Tiffany Taft, PsyD, MIS

Emerging research shows that changes in the body's blood sugar or "glycemic variability" may worsen inflammatory bowel disease (IBD) symptoms such as nausea, bloating and pain. Dr. Taft hopes to first determine if glycemic variability is linked to symptom severity in patients with IBD and secondly, identify how the foods IBD patients eat affect their glycemic variability. Study participants will wear a continuous glucose monitor, like those worn by patients with diabetes, for 14 days to assess changes to their blood sugar levels. During this time period, participants will write down their daily IBD symptoms and complete a journal of what they ate and drank to detail their diets. The diet information from the food journals will be entered into a nutrition analysis software program to identify what, if any, aspects of the person's diet affect their blood sugar, and how changes in blood sugar might affect their IBD symptoms. Understanding glycemic variably offers a novel approach to the diet puzzle to better managing IBD.

Correlation of Cell Types Other than Eosinophils with Esophageal Distensibility in Children with Eosinophilic Esophagitis

Principal Investigator: Joshua Wechsler, MD, MS

Eosinophilic Esophagitis (EoE) arises when foods trigger an allergic response in the esophagus. Chronic inflammation in the esophagus can lead to fibrosis (scarring) and then esophageal stiffness and narrowing. Patients experience difficulty passing food and impaction when food becomes trapped in the esophagus. Identifying early signs and drivers of scarring would help prevent the development of these and other serious complications. Endoscopic Functional Luminal Impedance Probe (EndoFLIP) is used to measure esophageal distensibility (stiffness or stretchiness). Prior research has demonstrated that eosinophils—a type of immune cell—have a weak association with esophageal distensibility. While different types of immune cells play a role in EoE, the association of non-eosinophil immune cells has never been studied. Dr. Wechsler plans to examine the correlation between esophageal distensibility and non-eosinophil immune cell populations in children with EoE. The team expects this work will guide future studies on EndoFLIP, as well as how immune cells such as mast cells and T-cells impact esophageal fibrosis to help develop targeted treatments for EoE.

Understanding How Chronic Inflammation Occurs in Gastroesophageal Reflux

Principal Investigator: Marie-Pier Tétreault, PhD

Gastroesophageal reflux disease (GERD) affects up to 27 percent of U.S. adults, resulting in more than 7 million patient visits annually. GERD leads to complications such as erosive esophagitis, Barrett's esophagus and esophageal cancer. Learning more about the molecular basis for the development and progression of GERD is critical to improving treatment options and decrease the risks for these esophageal conditions. Dr. Tetreault will look at the role of the crucial mediator of inflammation IKKβ in the development of chronic GERD. The team will use molecular approaches to shut down the expression of IKKβ and evaluate the impact of this loss on the development of GERD. This project will also employ a new technology called single-cell RNA sequencing (scRNA-seq) that enables the rapid determination of the precise gene expression patterns of tens of thousands of individual cells. Employing scRNA-seq should help give greater insight into how IKKβ signaling impacts the regulation of the inflammatory process in chronic gastroesophageal reflux.

A Window into the Liver: Markers in the Blood to Attempt to Predict Relapse in Autoimmune Hepatitis

Principal Investigator: Josh Levitsky, MD

No one knows precisely what causes autoimmune hepatitis (AIH) or why it leads to one's own immune system attacking itself, specifically the liver. Standard treatment focuses on suppressing the immune system with medications. Yet immunosuppressants have many side effects. General recommendations call for patients to stop taking the medications when they are no longer needed. Unfortunately, without them, most patients soon relapse and risk more liver injury. Currently, tracking relapses requires taking a biopsy of the liver—a very invasive procedure—and looking at it under the microscope. The Levisky lab believes that measuring levels of biomarkers in the blood may offer a better and less invasive window into the liver to predict AIH relapse earlier before the liver incurs any damage. This project offers the potential for better monitoring of patients with AIH. It also may shape the future of personalized treatments to individualize immunosuppressant therapy based on using simple blood draws rather than liver biopsies.

Can a Probiotic that Promotes Resilience to Sleep Disruption and Acute Stress Exposure Protect against Intestinal Inflammation in a Mouse Model of Colitis?

Principal Investigator: Fred W. Turek, PhD

Alterations in the intestinal bacteria (microbiome) and abnormal host responses to these bacteria may be contributing factors to the development of inflammatory bowel disease (IBD). Recent studies have revealed links between the microbiome, circadian rhythms and the sleep-wake cycle. Experiments in animal models of IBD have shown that disruption of sleep and circadian rhythms increases susceptibility to intestinal inflammation. In addition, studies in patients with IBD have found alterations in the circadian clock that may indicate pervasive sleep problems. Despite these connections, little is known about how sleep and circadian rhythms are involved in gut health or if strategies to promote sleep and reduce stress can mitigate the risk for intestinal inflammation. In previous work, Dr. Turek's team found that a probiotic promoted resilience to sleep restriction and acute stress exposure. In this project, the investigators hope to determine if a probiotic can also protect against intestinal inflammation and pathology in a mouse model of colitis.

Collection and Storage of DNA Specimens to Enable Future Validation of a Risk Prediction Tool that Uses Genetic Information to Reliably Predict Risk for Colorectal Cancer in the Local Population

Principal Investigator: Mohammad Ali Abbass, MD

While colorectal cancer is the second most common cause of cancer-related death in the United States, it is also largely preventable with screening. The Abbass team will identify a genetic tool based on blood samples that can accurately predict an individual's lifetime risk for developing colorectal cancer. The researchers will use DNA extracted from blood specimens obtained from patients at Northwestern Medicine with or without colorectal cancer. They will then evaluate changes that occur in the DNA building blocks to validate a polygenic risk score established for European patients. The aim is to use this score to identify patients who lack a family history for colorectal cancer but should potentially begin their colorectal cancer screening before 45 years of age—the current standard of care. The project could lead to a larger scale study that would target a more expansive population to initiate earlier screening in selected patients and decrease colorectal cancer-related deaths in younger patients.

Can a Personalized Exercise Program with Frequent Check-ins Improve Physical Conditioning and Survival in Patients Evaluated for Liver Transplantation?

Principal Investigator: Daniela P. Ladner, MD, MPH

Deconditioned patients with cirrhosis frequently experience worse outcomes before and after liver transplant. Exercise helps reduce frailty and leads to better outcomes, but patients face a variety of financial and logistical barriers to the regular physical activity needed to maintain strength. Additionally, transplant teams often expect patients to optimize their physical health on their own with little guidance. The Ladner team proposes a practical and affordable approach to enhance the physical conditioning of patients in the pre- and post-liver transplant setting. The researchers will develop a simple and cost-effective intervention called LIFT (Liver FrailTY). The intervention will include a full in-person strength assessment, an exercise program with smart phone guidance and remote coaching. Regular and frequent check-ins will be essential to encouraging patients to achieve recommended levels of exercise. Dr. Ladner's study will then measure the impact of LIFT on strength as well as positive clinical outcomes such as reduced mortality and fewer hospitalizations.

Functional Studies of a New Genetic Risk Factor (CLDN2) that Increases Pancreatitis Susceptibility

Principal Investigator: Beatriz Sosa-Pineda, PhD

Pancreatitis is an inflammatory condition that carries considerable socioeconomic burden. Often developing in middle-aged to elderly individuals, pancreatitis is responsible for the majority of gastrointestinal disease-related hospital admissions. Although acute to chronic pancreatitis susceptibility results from a combination of genetic, metabolic and environmental factors, it remains challenging to predict the onset, progression and severity of the disease. Understanding how distinct genetic risk factors affect the pathologic outcome in pancreatitis is key to developing better diagnostic and therapeutic tools. The Sosa-Pineda team will begin to dissect the role of claudin-2 (CLDN2), a newly identified pancreatitis risk factor, in pancreatic ductal cell function and pancreatitis outcome. The investigators will use an animal model for these new studies that will complement previous results from Dr. Sosa-Pineda's lab using CLDN2 knockout mice and ductal cell cultures. The investigators expect to demonstrate that sustained expression of this gene exacerbates tissue injury such as inflammation and fibrosis in chronic pancreatitis.

TOGETHER ON THE TERRACE

June 5, 2021 • Museum of Contemporary Art Chicago

Photos from left to right: Guests mixing and mingling inside the MCA; AB members Julie Kaviar, Erin Drain, Kate Hrad; Dr. Stephen Hanauer, Dr. John Pandolfino, Dr. Scott Strong; Denise and Jason Press, AB president.

View all the photos from this event here!

SAVE THE DATE!

SATURDAY, JUNE 4, 2022

Four Seasons Hotel Chicago

OUR DIRECTION

We are helping to transform digestive disease into digestive health for patients and families by generating resources to accelerate medical discoveries.

Thank You!

The DHF Ambassador Board thanks you for your support of "Together on the Terrace" and our mission to transform digestive disease into digestive health for patients and families at the Northwestern Medicine Digestive Health Center.

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