

M.I.R.I.A.D. Biobank

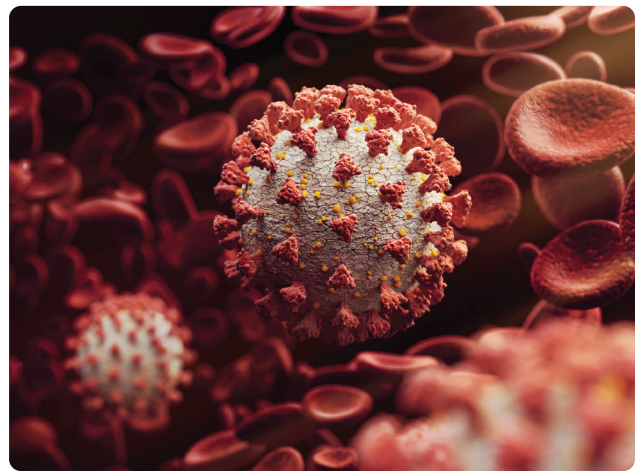
Material and Information Resources for Inflammatory and Digestive Diseases

A newsletter about research at Cedars-Sinai IBD

MIRIAD Biobank Researchers Use Big Data to Model U.S. Coronavirus Impact

by Dermot McGovern, MD, PhD

Researchers in the IBD Translational Research group, directed by Dermot McGovern, MD, PhD, have been using their “big data” skills to estimate the effect of the novel coronavirus caused COVID-19 pandemic. Using data generated from research on samples provided by MIRIAD research volunteers, McGovern’s team is using sophisticated data analytics to understand how this infection might affect patients with IBD. This work shows the true power of a biorepository such as MIRIAD and how participating in MIRIAD makes a difference, by allowing us to react quickly to a new medical question using the data we have already generated. In this way everyone who has provided us with samples is contributing to the effort to combat this disease.



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SPECIAL Coronavirus/COVID-19 Section

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Cedars-Sinai IBD Center Transforms to Meet Patient Needs Despite Coronavirus Restrictions

by Gil Melmed MD, MS and Shervin Rabizadeh MD, MBA

The coronavirus pandemic has posed challenges and opportunities to our IBD clinical operations and MIRIAD Biobank activities. While the challenges have caused disruption in our usual ability to deliver care, we have quickly pivoted to meet them. Our dedicated staff and faculty continue to provide the highest quality care for all of our patients despite these trying circumstances.

Our general message to our patients is to continue all IBD medications, and to follow public health advisories for those at increased risk for infection.

As the region's largest IBD center, we typically see hundreds of patients monthly in our ambulatory IBD clinics, in addition to our very active procedure units and surgical services. In response to the public health crisis, we are postponing all nonurgent procedures and in-person visits. As an alternative care-delivery mechanism, we are now able to offer telehealth visits for many patients. Critical procedures and visits (including research visits for those in clinical trials) continue to take place with appropriate precautions for both patients and providers. Our staff and providers have handled thousands of calls and electronic messages in a very short period of time, with the goal of providing clear and accurate information and guidance to our patients—many of whom are at increased risk for infection due to age, medications and other factors.

We are in constant communication with IBD centers around the world, who have come together to share information, guidance and updates about management of IBD in the setting of the COVID-19 pandemic. Our general message to our patients is to continue all IBD medications, and to follow public health advisories for those at increased risk for infection. Fortunately, the global experience thus far does not suggest an increased risk for COVID-19 complications for people with IBD, but we continue to learn more daily.

We look forward to resuming our usual operations as soon as we can safely do so, and in the meantime our team of clinical providers and staff is working diligently to continue uninterrupted care for all of our patients, and remain available to those who seek our care and guidance.

MIRIAD Biobank Making a Difference for People With IBD: IBD Psychosocial Program

by Amy Mann and Edward Feldman, MD

Emotional factors have a significant impact on patients and families of those with inflammatory bowel disease (IBD). Life stressors create a roller coaster experience for everyone, but those with IBD have additional issues to contend with that can either lead to or worsen anxiety and depression. Sleep disorders, fatigue and pain can increase the burden even more.

Depression, stress and anxiety can also influence patients' adherence to treatment plans.

Why is there such an impact? The answer is still not completely understood. While genetics are a likely component to the anxiety and depression, the uncertainty that accompanies illness is in itself a major stressor, and having IBD is associated with marked uncertainty. An ever-present set of questions naturally accompanies a diagnosis such as IBD: How will I feel? Will the medications I take affect me in ways that are disturbing or frightening? Will I need surgery, and if so, how will it affect my body image, my confidence, my dignity? Will I be able to finish my studies and or function in the workplace? Will I be loveable? Will I have sufficient energy to function? Will I constantly be

seeking access to a toilet? Will I pass this disease on to my children? These concerns come with their own question of whether emotional stress contributes to the severity of symptoms of IBD.

The Psychosocial Program within the Cedars-Sinai IBD Center, under the direction of Edward Feldman, MD, is focused on identifying those patients who require assistance with social needs regarding, for example, school, work and/or insurance issues, as well as identifying which patients are clinically depressed and/or are having difficulty managing anxiety. Counseling, education and sometimes referrals to appropriate specialists are then made available.

In order to identify patients who are in need, the Psychosocial Program team has devised and validated a brief but effective (and now in a digital format) health measures questionnaire. The questionnaire is scored automatically, and results are made immediately available to Amy Mann, a clinical social worker in our program for more than 10 years. These assessments and interventions are designed to have a positive effect on patient care and also physician and nurse satisfaction. Depression, stress and anxiety can also influence patients' adherence to treatment plans. By addressing these issues proactively, we will reduce unnecessary emergency department visits, imaging studies and hospitalizations.

The Psychosocial Program offers a seminar series for ongoing education of physicians in the evaluation and management of psychological complications. Residents and fellows training in the treatment of IBD at Cedars-Sinai also take part in these educational opportunities.

With the help of our many patient-participants, MIRIAD Biobank researchers are working to better understand the role of psychological factors in relationship to genetics and also the microbiome (communities of microbes that reside within the gut). There is much yet to be learned.

IBD Clinical Research and Clinical Trials

by Gil Melmed, MD, MS

The past couple of years have been very exciting due to newly approved treatments for IBD. In May 2018, the oral drug tofacitinib (Xeljanz®) was approved for moderately to severely active ulcerative colitis; this is the first “JAK-inhibitor” to be approved for IBD. In October 2019, the drug ustekinumab (Stelara®), previously approved for Crohn’s disease, was approved for ulcerative colitis; this is the first “anti-IL12/23” drug for IBD. The discovery and development of each of these therapies has spawned the development of multiple “next-generation” drugs, as there are clinical trials now being conducted for nearly a dozen additional JAK inhibitors and anti-IL12/23 inhibitors that may confer even greater advantages over the currently approved therapies.

MIRIAD participants play an important role in IBD clinical research...that can lead to the discovery of new “targets” with the possibility of becoming new drugs.

The current drug-approval pathway is complex. The Food and Drug Administration (FDA), the governing body that oversees drug approvals in the U.S., requires short- and long-term clinical trials to establish the safety and efficacy of new agents before they are approved. Clinical trials for IBD typically include colonoscopy assessments of disease activity in addition to symptom and quality-of-life assessments over the course of weeks or even years, depending on the specific drug and time course being studied. While the FDA still requires placebo-controlled trials in IBD, newer designs of many of the current clinical trials have mechanisms in place that allow study participants to get the “real” drug at some point in the study, even if initially assigned to receive placebo—although many trials are conducted in a “double blind” fashion, where neither the participant nor the doctor has knowledge of the specific treatment to which participants are randomly assigned. The

rules and regulations around clinical trials are set by the FDA, and centers who perform clinical trials have significant resources dedicated to the safe and compliant administration of research studies.

At the Cedars-Sinai IBD Center, Gil Melmed, MD, MS, director of IBD Clinical Research, leads a full-time clinical trial team experienced in the administration of studies for Crohn’s disease, ulcerative colitis and pouchitis. Melmed and the Cedars-Sinai IBD Center have participated in clinical trials for nearly every approved new drug for IBD over the past 25 years, including trials of Remicade®, Humira®, Tysabri®, Entyvio®, Stelara®, Xeljanz® and more. We are very selective about the trials that we take on, and every trial opportunity that comes to us undergoes thorough internal evaluation to determine whether it will be a good fit for our program and our patients. Through our clinical trials program, we are able to offer access to the latest in novel therapies, including newer drugs that may be safer or more effective than existing treatment options. If you feel your current treatment strategy may not be working for you and you are interested in hearing about the clinical trials for which you may be a candidate, talk to your doctor or contact us at 310-423-4100.

MIRIAD participants play an important role in IBD clinical research by donating tissue for laboratory experiments and providing clinical data that can lead to the discovery of new “targets” with the possibility of becoming new drugs.

FAQ: Answers to the Most Common Questions About Participating in the MIRIAD Biobank

by Dermot McGovern, MD, PhD

IBD Center clinicians and MIRIAD research coordinators are happy to answer questions when they talk with patients, accompanying family members and friends about participation in the MIRIAD Biobank. McGovern, director of IBD Translational Medicine, shares the most commonly asked questions and the answers:

Question: **If I participate in the MIRIAD Biobank, how will my samples and information be used?**

Answer: There are many ways to participate in MIRIAD. Whether you choose to donate samples, or prefer just to answer questions, the samples and information are used to support a wide array of IBD-related research projects aimed at understanding what causes IBD and also in the development of better treatments for the disease. The focus of the projects ranges from:

- Studies to understand the role of genetics in determining who will develop IBD and the unique features of individual subtypes of disease.
- Research to understand how genes interact with the billions of microbes in your gut (your microbiome).
- Investigations of the role of the immune system.
- Studies to show how genes, the microbiome and the immune system come together and cause inflammation leading to the discovery of new drugs to treat IBD.

Question: **Who is going to see my personal information?**

Answer:

- The privacy of MIRIAD participants is our priority, and personal information is secured behind a firewall.
- When information is shared with researchers, all information that could identify participants is removed and replaced with a code. A very limited number of authorized individuals can access the code.
- Research information is not shared with insurance companies or anyone outside research (unless as is required by law).

Question: **What has been learned so far from research participation?**

Answer:

- MIRIAD participation has been used to develop new ways to diagnose and ways to optimize treatment.
- MIRIAD participation has been used to develop new drugs and to identify other opportunities for treatments that are currently under investigation.
- Participants can see results of research involving MIRIAD participants in the articles posted in the clinic corridor and we are always happy to share copies of the articles—please ask us if you are interested.
- The MIRIAD Biobank Newsletter features progress in research by the scientists it supports.
- While we are not allowed to share individual results, including genetic data, we can discuss research findings as an overall summary with participants.

Integrative Medicine for IBD, Part 1: Complementary Therapies

by Eric Vasiliauskas, MD

The terms “alternative” and “complementary” medicine are often used interchangeably when referring to therapeutic approaches including herbal products, dietary and other supplements, and mind-body practices not currently considered to be part of traditional western medicine. The National Center for Complementary and Integrative Health describes “alternative medicine” as the use of non-mainstream products and practices in place of conventional medicine, whereas “complementary medicine” refers to using non-mainstream approaches together with conventional treatment.

The concept of “integrative medicine” attempts to bring conventional and complementary approaches together in a coordinated way with an emphasis on the importance of nutrition, exercise, stress management and a strong support network.

Cedars-Sinai IBD Center faculty member, Eric Vasiliauskas, MD, director of the Nutrition and Integrative IBD Program has a long-standing interest in complementary and integrative medicine and seeks the proper blend of complementary and conventional regimens tailored to the needs of individual patients.

Is there a role for complementary medicine in IBD?

There have been many exciting medical advances in the field of IBD over the last two decades. Clinical trials tend to focus more on addressing active IBD symptoms. Studies with biologic and other newer therapies demonstrate significant response and remission rates, and can be life-altering, but the reality is that longer-term outcomes and real-life experiences are still not as robust or durable as we would like. Many prescribed medications help patients feel better, but not always truly well. Even though the gastrointestinal symptoms may be much better, other symptoms may persist, including fatigue, anxiety, depression, joint pains, bone problems, mouth ulcers, poor appetite, etc. Adding complementary interventions to the treatment can potentially help address many of these persisting issues.

In conventional medicine, the concept of “prevention” often translates to “maintenance therapy,” which typically involves continuing the medication regimen that seems to be helping with gastrointestinal symptoms, a large portion of which involve long-term immunosuppression. Many complementary interventions focus more on promoting a comprehensive healthy lifestyle encompassing physical, mental, emotional and spiritual wellness—thereby potentially improving quality of life, helping address medication-associated side effects and potentially reducing longer-term medication exposure.

Complementary Medicine Considerations

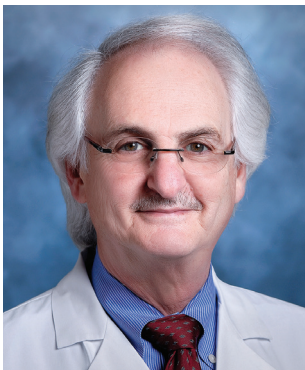
- It is important to consider the goal of any given therapy or intervention. Is it to turn off the inflammation or to address specific symptoms, side effects or other manifestations?
- It is critical to understand the concept that symptom control (feeling better) does not equate to adequate disease control, and that not treating inflammation adequately can predispose patients to complications such as strictures, perforation, malnutrition, poor growth and even cancer.
- Not everything that is “natural” is “safe,” especially if pursued long-term. When considering any therapy, it is important to weigh the short-, as well as, long-term risks and benefits.

While both traditional and complementary therapies can work to varying degrees, in some cases really well, it is important to recognize that in many instances any single intervention is unlikely to achieve optimal long-lasting wellness on its own. Thus, a thoughtful, proactive, integrative approach may offer the best chance of not only feeling better, but feeling really well—and staying that way.

Note: This edition of the MIRIAD Biobank Newsletter begins with an overview of the complementary approaches proposed for IBD. In future MIRIAD Biobank newsletters, we will continue to explore the various complementary options and considerations in more detail.

MIRIAD Biobank Team Spotlight:

Meet Edward Feldman, MD, and Amy Mann of the IBD Psychosocial Program



Meet Edward Feldman, MD

Edward Feldman, MD, is a professor of Medicine at Cedars-Sinai and a member of the Cedars-Sinai IBD Center since its inception in 1992. He attended medical school at the University of Indiana, completed his internship at the Wadsworth VA Hospital along with several other physicians who, like Feldman, would go on to become the leaders of the field. He completed his residency at Harbor General Hospital and gastroenterology fellowship at UCLA. Feldman was early to recognize the significant psychosocial impact to patients with IBD, thus sought additional training at the Los Angeles New Center for Psychoanalysis. Feldman has trained generations of young physicians, many of whom followed in his footsteps to specialize in gastroenterology and IBD. With this combination of expertise in gastroenterology and psychology, Feldman is ensuring that

our patients' bodies and minds get the care they need. When not working with people with IBD, Feldman enjoys his family and his daily yoga practice.



Meet Amy Mann

Amy is a licensed clinical social worker in the IBD Center and team member for more than 10 years. Amy works with both pediatric and adult people with IBD. She earned her undergraduate degree in psychology and creative writing from the University of Southern California, and received her master's degree in social service administration and policy from the University of Chicago.

She provides psychosocial assessment and intervention in the outpatient IBD clinics for biological, psychological and social factors, and she connects patients to supportive services. She is actively involved in IBD research, co-authoring multiple articles on IBD and quality of life. Amy recognizes IBD can include emotional and psychological challenges which can affect all areas of life, not only physical health. She encourages

various healthy coping techniques—including behavioral treatment and stress reduction—facilitates a monthly support group and refers for psychiatric medication consultation, if desired. She knows an IBD diagnosis can touch the lives of not only the patient, but those who surround and love them.



Featured Research Study: Rnaset2 Defines a Subgroup with More Severe Crohn's Disease

By Rivkah Gonsky, PhD

Ribonuclease T2 (RNASET2) gene and its protein play a role in inflammation and are the subject of a very promising line of investigation led by Rivkah Gonsky, PhD. Gonsky has discovered that patients with Crohn's disease who carry gene abnormalities associated with decreased amounts of RNASET2 protein develop a more severe, drug-resistant form of disease. She also found a relationship among these RNASET2 gene, and two other IBD-associated genes known as TNFSF15 and ICAM1. Interplay of the genes leads to reduced RNASET2 levels, resulting in increased inflammation. Conversely, increasing RNASET2 protein levels leads to reduced inflammation. Based on these exciting results, Gonsky and colleagues are in the process of developing a diagnostic test to identify patients who are likely to be successfully treated with the RNASET2 protein as a single treatment or as part of combination therapy.

These results would not have been possible without the partnership of MIRIAD Biobank participants who contribute to exciting research by donating blood and/or allowing discarded tissue from surgeries to be used by researchers.

Important Numbers and Contact Information

- **Adult patient appointments:**
310-423-4100
- **Pediatric patient appointments:**
310-423 -7100
- **MIRIAD Biobank information:**
310-423-3550
- **Email address:**
miriad.ibdbiobank@cshs.org
- **MIRIAD Biobank webpage:**
cedars-sinai.org/research/departments-institutes/ibiri/miriad-ibd-biobank.html
- **Cedars-Sinai IBD clinical webpage:**
cedars-sinai.org/programs/digestive-liver-diseases/clinical/ibd-center.html
- **Pediatric IBD clinical webpage:**
cedars-sinai.org/programs/digestive-liver-diseases/clinical/ibd-center/pediatric.html
- **IBD Clinical Trials:**
cedars-sinai.org/programs/digestive-liver-diseases/clinical/ibd-center/clinical-trials.html
- **Follow us on Twitter:**
[@IBDCedarsSinai](https://twitter.com/IBDCedarsSinai)

Click here to watch a video with more information about MIRIAD Biobank Participation:

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