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

<u>Material and Information Resources for Inflammatory And Digestive Diseases</u>

A Newsletter about Research at Cedars-Sinai IBD

FMT and IBD

What is FMT?

FMT (Fecal Microbiota Transplant) has generated quite a bit of buzz in the media over the last couple of years. In this article we describe FMT and discuss its potential utility in IBD.

FMT involves the collection of fecal matter from a healthy donor, and putting it into a recipient. The fecal matter is typically infused into the colon by colonoscopy, but it can also be administered via enema or even in new encapsulated pills by mouth. FMT has been around a long time, but regained popularity with the resurgent interest in the microbiome and its potential effects on gastrointestinal health and disease. The concept is that intestinal infections and perhaps other diseases of the gut and the body relate to abnormal proportions of "good" and "bad" bacteria and other microbial components that normally reside in the intestine. FMT involves restoring the "healthy" balance of these good and bad bacteria in your intestine by transferring fecal bacteria from another individual. This has the potential to treat disease.

FMT has been shown to be effective and safe in the treatment of recurrent Clostridium difficile infection and is increasingly gaining acceptance among both patients and physicians.

Is FMT a Good Treatment for IBD?

We currently do not know whether FMT cures or treats IBD. Interestingly, FMT appears to be beneficial for treating Clostridium difficile infection in patients with both IBD and a Clostridium difficile infection. However, in that scenario, FMT treats the infection, not the underlying IBD.

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The risks and benefits of treating IBD with FMT are still emerging. Most of the studies to date have not been placebo-controlled and have focused on medically resistant patients with severe cases of IBD. The evidence is conflicting as to which patients might benefit and which patients will not. In fact, some patients with IBD have experienced worsening of their disease, with flares triggered by FMT.

There are many unanswered questions about FMT for IBD that require further research.

- Why does FMT for IBD lead to improvement in some individuals, but worsening of disease in others?
- For FMT to work for IBD, is it a one time administration, or multiple administrations over time (like most medications)?
- Does FMT work differently for Crohn's disease than for ulcerative colitis?
- Does FMT work differently depending on which parts of the intestines are affected by IBD inflammation?
- Are there factors that make certain donor stool more appropriate for IBD treatment?
- Does FMT for IBD require that we "tailor" the donor microbiome to the recipient, in a precise / personalized way?
- How do the genetics of the individual with IBD influence the ability to respond?
- Does diet play a role in whether FMT is effective?

At Cedars-Sinai, we have a team of researchers dedicated to understanding the microbiome and the effects of FMT in health and in disease.

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MIRIAD IBD Biobank - Making a difference for people with IBD.

The National Institutes of Health recently awarded Cedars-Sinai IBD \$10,000,000 for research on the genetic and immunologic causes of IBD. This 5 year award is the latest to be funded in a 25 year continuous grant and the longest IBD study of its kind. Starting in 1992, in addition to support for research projects, this grant provided dollars to set up a repository of IBD samples at Cedars-Sinai. That repository ultimately became known as the MIRIAD IBD Biobank. Over the quarter of a century that the MIRIAD IBD Biobank has been in existence, almost 20,000 people with IBD have donated one or more specimens for research purposes.

In addition to continued funding for the MIRIAD IBD Biobank, four related research projects were also funded to study exciting new concepts in genetics of IBD and the interface between the microbiome and the immune system. The team of investigators includes Dr. Stephan Targan, Dr. Dermot McGovern and Dr. David Underhill from Cedars-Sinai, and also Dr. Mitchell Kronenberg from La Jolla Institute for Allergy and Immunology and Dr. Jonathan Braun from UCLA. This long-standing effort has resulted in many IBD research breakthroughs. With the continued support of MIRIAD IBD Biobank participants, more advances are sure to come over the next few years. Thank you for being a research partner of Cedars-Sinai IBD.



Vaccinations and IBD

New guidelines about vaccinations have been released by the American College of Gastroenterology. Research performed by Cedars-Sinai IBD physician/scientist Dr. Gil Melmed and an international team of colleagues showed that people with IBD may not be receiving the appropriate amount of preventive care, and these guidelines call for gastroenterologists to partner with primary care physicians to make sure that health maintenance issues are being addressed.

IBD and Vaccinations FAQ:

Should I get a flu shot?

YES! All children and adults should get a flu shot This includes those with or without IBD. The flu shot is safe and effective even if you are taking immunosuppressive therapies. Those with IBD who are on immunosuppressive therapies should specifically receive the flu "shot", but should avoid the live inhaled "FluMist" vaccine.

Should I get a pneumonia shot?

If you have IBD, you should get a pneumonia shot. There is a higher risk of pneumonia in people with IBD. There are 2 forms of the pneumonia vaccine (Pneumovax[®] and Prevnar[®]), and if you are an adult on immunosuppressive therapies you may need one or both of these vaccines to provide the best protection against pneumonia.

Should I get a tetanus shot?

All adults should receive a tetanus booster vaccine every 10 years, regardless of whether they have IBD and whether or not they are on immunosuppressive therapies. Furthermore, in many states there is currently a pertussis ("whooping cough") epidemic; the pertussis vaccine is administered as part of the tetanus booster vaccine (called "TDaP") and can provide important protection against this epidemic infection.

Did my childhood vaccinations cause me to develop IBD?

There is no credible evidence that childhood vaccinations cause or contribute to IBD development.

Should my child with IBD be vaccinated for mumps and measles?

Mumps and measles infections can be fatal even in healthy children, and can spread in communities where vaccination rates are lower. The "anti-vaccination" movement is based on faulty evidence suggesting an association between measles vaccination and autism. This evidence has been retracted by the original authors, and has been soundly "debunked" in dozens of scientific and scholarly publications over the past 20 years. There are rare exceptions for when the measles and mumps vaccinations should be withheld because they are live virus vaccines, such as in cases when children with IBD are already on immunosuppressive therapies. It is important that all other people around these more vulnerable children are appropriately vaccinated in order to provide "herd immunity" where a community is protected from these devastating infections when the vaccination rate in the community overall is very high.

Do drugs such as biologics, Azathiopirine, Imuran or methotrexate affect my resistance to infection?

Yes. These drugs can interfere with the body's ability to naturally fight infection and theoretically increase risks for infections. Furthermore, these infections might be worse in the setting of being on one of these medications. Therefore, it is all the more important to ensure that we do what we can to prevent preventable infections by following vaccination recommendations. The vast majority of vaccines are not live vaccines, and are thus safe to administer regardless of whether or not someone is on immunosuppressive therapies. For live vaccines, you should have a discussion with your doctor about weighing the relative risks and benefits of vaccination in the setting of being on (or temporarily stopping) these IBD drugs.

What are examples of live vaccines?

Most vaccines are NOT live vaccines. Live vaccines that should generally be avoided in individuals on immunosuppressive therapies include the live FluMist, measles/mumps/rubella, chicken pox (varicella), and shingles (zoster) vaccines.

What other vaccinations should I ask my doctor about?

Whenever travelling outside the country, it is important to check with your doctor about recommendations for the country/location you are visiting. It is also a good idea to make sure your gastroenterologist is communicating with your primary care doctor/internist in order to make sure that you are up-to-date with current health maintenance recommendations.





Meet IBD Physician Gil Melmed, MD

Director of Clinical Inflammatory Bowel Disease and Director of the Advanced IBD Fellowship

Dr. Melmed is a physician/scientist trained both in IBD and also in clinical study design, which means that the clinical research done at Cedars-Sinai IBD is optimized to provide credible and reliable results. Dr. Melmed is interested in the quality of the care provided to individuals with IBD and making sure that patients everywhere receive the highest possible standard of care using evidence-based approaches. The management of IBD is complex, given the nuances of the different forms of the disease and the available treatment options; improving the quality of care in a standardized way is thus a challenging task. Dr. Melmed and his colleagues have developed a nationwide program to help all types of practices learn how to improve care. His research interests are clinical and surgical outcomes, quality of life, and quality of care.

Dr. Melmed is an internationally renowned expert in the role of immunizations/ vaccinations in the context of preventing infections in people with IBD (see FAQ on Page 3).

Dr. Melmed is also devoted to the development and training of other physicians to become experts in the treatment of IBD. As the Director of the Cedars-Sinai Advanced IBD Fellowship, Dr. Melmed mentors gastroenterologists to learn "The Cedars-Sinai Approach" to treating ulcerative colitis and Crohn's disease.

Dr. Melmed received his bachelor's degree from the University of Pennsylvania and his medical degree from Albert Einstein College of Medicine. He completed his residency at Cedars-Sinai Medical Center and his gastroenterology fellowship at UCLA, where he also received a master's of science in Clinical Research.



Meet MIRIAD IBD Biobank Clinical Research Associate, Gil Barron

If you have had an endoscopy procedure at Cedars-Sinai, there is a very good chance you have met Clinical Research Associate Gil Barron. He has been part of the team for more than five years and is responsible for coordinating research projects between patients, care team members and other research staff. You are most likely to see Barron when he is asking your permission to collect samples for the MIRIAD IBD Biobank and/or various other research projects. Since his start in 2011, most of the projects he has been involved with dealt with the microbiome, which in recent years has become a hot topic in IBD research.

Feel free to ask him any questions you might have regarding the microbiome – or hiking trails. He is quite knowledgeable about both.



Featured Research Project supported by participants of the MIRIAD IBD Biobank Immune Responses in Inflammatory Bowel Disease

Dr. Kathrin Michelsen

The causes of IBD are not well understood. Recent research suggests hereditary, environmental factors and the immune system contribute to the development of IBD. The immune system usually attacks and kills foreign invaders, such as bacteria, viruses, and fungi. Under normal circumstances, the harmless bacteria and fungi in the gut coexist peacefully with the immune system. However, in people with IBD, these bacteria and fungi are mistaken for harmful invaders and the immune system mounts a response leading to inflammation of the intestine. In IBD, the inflammation becomes chronic and can lead to ulceration, thickening of the intestinal wall, and eventually causing patient symptoms.

Research shows that patients with Crohn's disease and ulcerative colitis have distinct immune responses and inflammation of the intestine. Recent reports have shown that genetic variations in certain immune genes contribute to the development of IBD and the severity of the disease. Our laboratory is interested in how genetic variation in immune genes lead to these distinct immune responses. Our study analyzed the blood of IBD patients and we found that patients that carry a "risk" variation for one immune gene have higher levels of this factor in their blood. Recently, we have linked this factor to a novel immune response that leads to intestinal inflammation. Our ongoing study uses laboratory technologies to analyze blood and small tissue samples from the gut of patients with IBD. If we can identify the patients that develop this immune response, we can develop better and more individualized treatments for patients with IBD.

CEDARS-SINAI IBD HAS TREATMENT TRIALS AND CLINICAL RESEARCH STUDIES ENROLLING RIGHT NOW!

Ask your physician about eligibility requirements.



Cedars-Sinai IBD 360° Watch the Video!



www.youtube.com/watch?v=KUiIsNXXqUI

Important numbers and contact information:

- Patient appointments 310-423-4100
- Research Project Information 310-423-3550
- Email address MIRIAD.IBDBiobank@cshs.org
- Cedars-Sinai IBD clinical webpage cedars-sinai.edu/ibd
- Cedars-Sinai IBD research webpage cedars-sinai.edu/Research/Departments-and-Institutes/IBD/index.aspx
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