

What's in Your Genes?

Research has identified about 240 gene variants that seem to be associated with IBD, but not a single one has been proven to actually cause the disease, says Andres Hurtado-Lorenzo, PhD, senior director of translational research at the Crohn's & Colitis Foundation. However, that may change in the not too distant future, as genetic research is advancing rapidly.

Since the Foundation's Genetics Initiative was founded in 2012, scientists have narrowed their focus to about 14 genes. "We're now studying these genes and mutations in these genes," says Hurtado-Lorenzo. "As we understand more about the mechanisms of how these gene variants lead to disease, we can come closer to prioritizing new targets for drug discovery."

Big Ideas Call For Big Data

You can't propel breakthroughs in science quickly without data — and lots of it. That's where the Crohn's & Colitis Foundation's IBD Plexus® comes in. A massive research exchange platform, IBD Plexus® contains data from over 20,000 patients with IBD. In fact, it's poised to become the single largest IBD database in the world.

What's so unique about IBD Plexus®, aside from its sheer size, is that the Foundation's research partners — including those in academia and the pharmaceutical industry — can dramatically accelerate their work by taking advantage of the biosamples and extensive data that have already been collected from thousands of patients across the country. "We have created a collaborative environment through the development of novel data-sharing guidelines, in which those who access IBD Plexus® resources have to give back to the community," says Angela Dobes, senior director of IBD Plexus®.

The result: researchers can analyze data at a scale that has never been explored in IBD and cut years off the research lifecycle. Learn more at crohnscolitisfoundation.org/IBDPlexus.

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FOUNDATION IMPACT

Leveraging Years of Major Foundational Research Investments
Our past research investments in important areas such as genetics and the microbiome, are paying off.

The Viral Connection

A number of studies using animal models have suggested that exposure to certain viruses might play a role in triggering the development of IBD. But which viruses are important, what is their role in humans, and can they also trigger a flare?

Lindsey Albenberg, DO, an attending physician at The Children's Hospital of Philadelphia, is hoping to answer these questions. She and her colleagues are working on research funded by the Crohn's & Colitis Foundation's Environmental Triggers Initiative to learn more about the impact of viruses on IBD. "Often, patients are doing well and then they develop a disease flare and we don't always understand why," she says.

To find out if a viral infection might be responsible for the shift, Albenberg's group is developing technology that looks for viruses — so far, they have a list of about 20 of them — in the blood of patients with IBD. The next step is collecting blood and stool samples of IBD patients at baseline, then following them and collecting a second set of samples if they flare. "We want to know if there are any new viruses in the blood that were not present when they were doing well," she explains.

Albenberg explains that they hope this research will yield insights that are relevant to current IBD patients, while providing valuable information that might one day be used to predict who will get IBD in the first place. "We know IBD involves genetic factors, but those only explain a small percentage of disease development," she says. "The theory about viruses is that you get an infection, your immune system becomes inappropriately overactive, and you can't get control of your immune response," which leads to autoimmune conditions such as IBD.

Help Us Change Lives

The innovative projects described in this edition of Under the Microscope are just a few of our endeavors designed to accelerate the pace of research and uncover new treatments and cures for Crohn's disease and ulcerative colitis as quickly as possible. While our ultimate vision is a world without IBD, we're equally committed to helping patients who are struggling with the physical and emotional toll of living with IBD right now, but we can't do any of it without your help.

Help create a better tomorrow for those suffering from IBD by making a gift to the Crohn's & Colitis Foundation today. To make a contribution to the Crohn's & Colitis Foundation, please visit crohnscolitisfoundation.org/microscope.

The Crohn's & Colitis Foundation would like to thank our President's Corporate Circle Members for their invaluable support.

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Learn more at crohnscolitisfoundation.org

The Crohn's & Colitis Foundation is the leading non-profit organization focused on both research and patient support for inflammatory bowel disease (IBD). The Foundation's mission is to cure Crohn's disease and ulcerative colitis, and to improve the quality of life for more than 3 million Americans living with IBD. Our work is dramatically accelerating the research process through our database and investment initiatives; we also provide extensive educational resources for patients and their families, medical professionals, and the public.

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Join the Founders Society

The Founders Society honors those who strengthen the vision and commitment of the Crohn's & Colitis Foundation by including the Foundation in their estate planning. As a member of the Founders Society you will be listed in our Annual Report, and receive inside information and updates regarding our mission advancement and research progress. We invite you to join the Founders Society today.

If you're interested in making a planned gift or have questions regarding planned giving and the Founders Society, please contact Allison Coffey at acoffey@crohnscolitisfoundation.org.

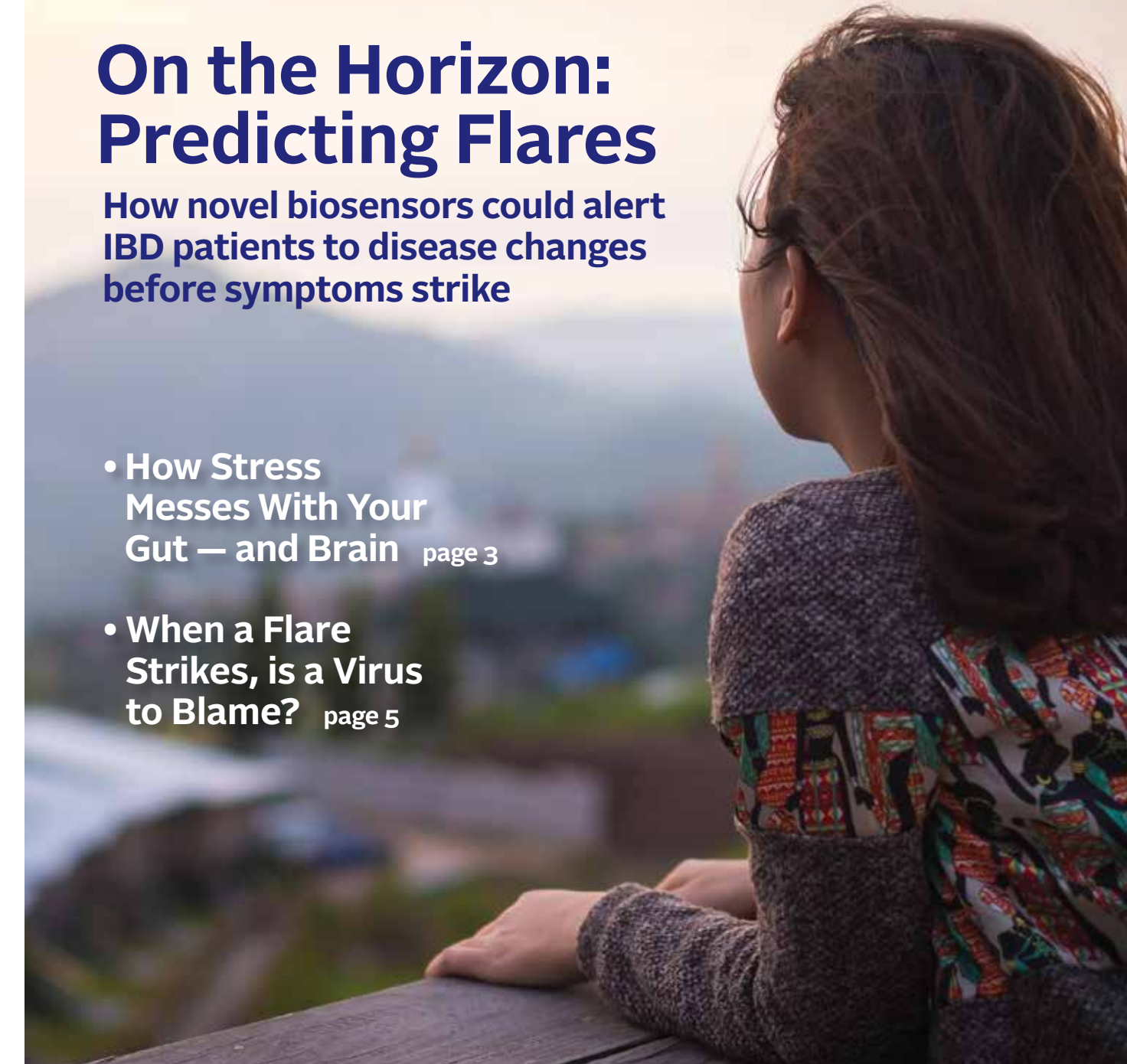


Under the Microscope
GROUNDBREAKING RESEARCH AND SUPPORT FOR PEOPLE WITH IBD
CROHN'S & COLITIS FOUNDATION
SPRING 2019

On the Horizon: Predicting Flares

How novel biosensors could alert IBD patients to disease changes before symptoms strike

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- When a Flare Strikes, is a Virus to Blame? page 5



Predicting Flares, Before They Start

One day, this could be a reality, thanks to the development of some novel biosensors that are currently being studied.

When a patient is in the midst of a flare, a doctor might be able to prescribe medication to stop it. But what if you could get an advanced warning that a flare was about to strike? You might be able to take action much sooner and maybe even prevent the flare completely.

Better than a Fitbit

Thanks to the support of the Crohn's & Colitis Foundation, scientists at the University of Texas, Dallas, are studying inflammatory biomarkers — measurable indicators of disease activity that are secreted in sweat. The first step: demonstrate that an innovative bracelet embedded with biosensors can detect specific biomarkers (such as C-reactive protein) that may be good predictors of an impending inflammatory bowel disease (IBD) flare.

"We already have sweat-sensing prototypes looking for other [substances] in sweat, such as alcohol, glucose, and cortisol, so the fundamental concept of sweat-based biomarker detection has been proven," says researcher Shalini Prasad, PhD. Once her team confirms that the same mechanism can be used to detect biomarkers linked to IBD flares, the hope is that patients could wear a bracelet and receive a notification that warns them of an impending flare. "It would be like a 'check engine' light on your car turning on," says Prasad. "Then the physician and

67%

of Crohn's disease patients currently in remission will relapse within eight years.*

The urgent need to address this and other patient challenges is the reason that the Crohn's & Colitis Foundation exists and why we're working, with your support, to find new and innovative treatments.

*Source: World Journal of Gastroenterology, October 2015

FOUNDATION IMPACT

Catalyzing Critical Research in New Domains


We are leading the way with millions of dollars of research investment in critically important areas of environmental disease triggers.

patient can get together and do some decision making. If you catch a flare before its onset, the treatment might become a lot less protracted." Prasad's team hopes to complete testing of the basic sweat-sensing technology within the next 24 months. They will then move to studies involving IBD patients with various levels of disease activity and coexisting conditions, such as diabetes or heart disease.

Gut Insider

What's going on inside your gastrointestinal (GI) tract? Right now, the best way to find out is to undergo an endoscopy and/or colonoscopy, which are invasive imaging procedures that require sedation. While those tests are expected to remain essential for the foreseeable future, scientists at the Massachusetts Institute of Technology (MIT) are working on creating a capsule that IBD patients could swallow (like a pill) to gain important information about the status of their condition and related risks, including colon cancer.

Researchers led by Timothy Lu, MD, PhD, have developed several versions of such a capsule, and they're planning to use funding from the Crohn's & Colitis Foundation to move their concept forward in IBD. "We've already built a capsule and tested it in the lab as well as in some pig experiments," says Lu. "We know it can detect bleeding, so we're confident that it works." Next, they'll aim to make it more sensitive and add sensors to detect inflammatory markers and gases that can be used to monitor IBD disease activity, as well as detect early signs of colon cancer. Lu's team is also considering integrating a camera into the capsule.

In the future, the plan is to have all the information collected by the capsule transmitted to a patient's smartphone, so getting a report about what's going on inside your body would be as easy as checking Facebook or sending a text message. "If we continue to get adequate funding, I'm optimistic that we'll be ready for the first human studies within three years," says Lu. 

You've Got Questions. We're Searching for Answers.



At the Crohn's & Colitis Foundation, one of our most important objectives is to inspire and engage patients. That's why we're working so hard to support projects that really matter to people living with IBD.

Q Does stress really increase the risk of flares?

A Absolutely, says Emeran Mayer, MD, PhD, a gastroenterologist, neuroscientist, and director of the G Oppenheimer Center for Neurobiology of Stress and Resilience at the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA. Mayer is quick to clarify that IBD is not "all in your head," but it's been well-established that stress can play a role in disease onset as well as flares, in combination with genetic and other risk factors and triggers. What's not totally clear is how stress alters brain function and, in turn, may influence the balance of microbes in a patient's gut in a way that has implications for disease activity.

To find out which mechanisms are responsible, Mayer and his team are getting ready to follow 100 patients with ulcerative colitis for one to two years, thanks to support from the Crohn's & Colitis Foundation's Environmental Triggers Initiative. Participants will be assessed at baseline — they'll have their gut

"We want to figure out if there are specific changes to the microbiome and in the brain when someone goes into a flare."

—Emeran Mayer, MD, PhD

microbes measured, blood tested, and they will also undergo brain imaging tests. They'll then repeat the same tests every three months, plus whenever they report that they're going into a flare.

Mayer's work is based on the hypothesis that chemical signals between the GI tract and the brain are key players during a flare. "We want to figure out if there are specific changes to the microbiome and in the brain when someone goes into a flare. That information might allow us to predict who would benefit from mindfulness treatment, cognitive behavioral therapy, or pharmacological therapy aimed at the brain in vulnerable patients, in addition to traditional treatment for IBD," says Mayer.

Q Can newly-diagnosed patients find out how their disease will progress?

A After getting an initial diagnosis and starting on treatment, some patients will have a disease that stays in remission, while others will be plagued by frequent flares. Determining who will fall into each camp has been a mystery, but a new blood test, PredictSURE IBD, may have the potential to change that. The test, which uses specific findings in a blood sample to tell patients whether they're at high or low risk of relapses, is about to hit the market in the UK.

According to research conducted in Europe, 91% of people who had multiple relapses within 12–18 months after taking the PredictSURE IBD test were correctly identified by the test as being in the high-risk group, and 98% of the low-risk group did not have multiple relapses, says Eoin McKinney, PhD, chief scientific officer of PredictImmune Ltd, the company that developed the test.

Will the test work as well in the U.S. patient population? That's what a new study funded by the Crohn's & Colitis Foundation will find out. A diverse group including people from the Northeast, Midwest, South, and West Coast will soon be recruited for the study. Results are expected in about two years.

This research is being supported by the Foundation's IBD Ventures Initiative, which is devoted to accelerating the pace of research by making investments in innovative products, treatments, and devices that have the potential to reach patients in the near future.

64%

of IBD patients say that their disease controls their life rather than the other way around.* We're working to change that.

*Source: 2018 U.S. UC Narrative, a collaborative survey between the Foundation and Pfizer of ulcerative colitis patients and gastroenterologists

Q Can I find out if my child is at high risk of fibrosis?

A Fibrosis, the hardening and thickening of the bowel wall, is a common IBD complication. If your child has been recently diagnosed with IBD, a doctor can order an IBD serology test, a blood test that estimates the risk of fibrosis over the next five years, says Ted Denson, MD, director of the Inflammatory Bowel Disease Center at Cincinnati Children's. However, that test is only about 70% accurate, and Denson, co-principal investigator of the Crohn's & Colitis Foundation's Pediatric RISK Stratification study, believes we can do better.

Support for the ongoing RISK initiative is key to the Crohn's & Colitis Foundation's commitment to leveraging our years of major investments and building upon them. Since its inception more than a decade ago, RISK investigators have enrolled more than 1,000 children with Crohn's disease at 28 centers in the U.S. and Canada, and successfully identified biological markers that predict more severe Crohn's complications in pediatric patients at diagnosis.

FOUNDATION IMPACT

Accelerating the Pace of Research

We are speeding the development of breakthroughs by supporting unique projects and innovative solutions that have the potential to change the lives of people with IBD.

At the moment, Denson and his colleagues are in the process of analyzing samples taken from the intestines of Crohn's patients during colonoscopies, so they can confirm a previously identified predictor called the "extracellular matrix gene signature." "When we combine the extracellular matrix information with the current blood test (IBD serology), we can predict fibrosis risk with about 80% accuracy," he explains.

In the future, there might be a third component that improves accuracy even further, perhaps by taking information from imaging tests (such as MRIs) and combining it with data from the extracellular matrix test and IBD serology test.

Accurately predicting fibrosis risk is crucial, because, right now, once it develops, the only fix is surgery. However, if a doctor knew that a patient was at a high risk, more aggressive treatment could be considered sooner. "Probably the worst thing you can do is use less effective therapies for a longer period of time, because more and more fibrosis builds up in the intestines," says Denson.

Q How can I participate in clinical trials or studies?

A We need your help to find cures. Visit our Clinical Trial Finder at trials.crohnscolitisfoundation.org.



Wondering what it's really like to take part in a study? Contact us at 800-932-2423 and ask to be connected to one of our Clinical Trials Ambassadors. 