

Treating IBD by Rebalancing the Gut Microbiome

Everyone has a mix of microbes in their gut, some of which are beneficial and others that can wreak havoc—especially in people with Crohn’s disease and ulcerative colitis. Thanks, in part, to funding through IBD Ventures, researchers at Vedanta Biosciences are currently developing a cocktail of several strains of living bacteria (a live biotherapeutic product, or LBP) designed to flood the gut with enough beneficial bacteria to outcompete a harmful strain (*Klebsiella pneumoniae*) and other bacteria that have been linked to IBD flares.

“*Klebsiella* typically lives in the mouth since it can tolerate a little bit of oxygen, but in IBD patients it’s often found in the intestines because inflammation may lead to increased oxygen levels,” says Bernat Olle, PhD, cofounder and chief executive officer

“IBD VENTURES is an **unprecedented game-changer**.”
—ANDRES HURTADO-LORENZO, PhD,
Vice President,
Translational Research Programs

of Vedanta Biosciences. Once *Klebsiella* and other harmful bacteria take root in the intestines, they kick off an immune response that leads to more inflammation and worsening symptoms.

“What we’ve been doing with the Crohn’s & Colitis Foundation is identifying and testing combinations of good bacteria that, together, can kick out the ones that cause inflammation,” says Olle. “We’ve already found combinations that work in mice, but we want to identify the optimal composition and number of bacteria before we advance to studies in humans to eventually develop a prescription drug.”

FOUNDATION IMPACT

Catalyzing Critical Research in New Domains

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

A Revolutionary Treatment for Fistulizing Disease

Fistulas—abnormal connections or channels between the intestines and other organs or tissues—develop in 35% to 50% of adults with Crohn’s disease. Despite how relatively common they are, fistulas are extremely hard to treat and even major surgery isn’t a solution for many patients. But a new putty-like gel could change that.

Late in 2019, the Crohn’s & Colitis Foundation reached an agreement to make an IBD Ventures investment in Tissium, a company that manufactures medical-grade putty that sticks in damp conditions and forms a vacuum seal that hardens when activated with light. The hope is that this compound will lend itself to plugging fistulas via a minimally-invasive procedure.

Tissium, which is based in France, has already received approval from European authorities to market a putty that’s designed to seal blood vessels during vascular surgery. Now the company is aiming to take that same basic formula and tweak it so that it can be used to seal fistulas in IBD patients who have developed this complication. Given the compound’s proven success elsewhere in the body, there’s good reason to believe it will work in the digestive tract.

The next step, which will take place thanks to the IBD Ventures investment, “is to conduct a proof-of-concept trial in an animal model to evaluate fistula healing,” says Maria Pereira, PhD, chief innovation officer of Tissium.

Thank you to all the members of our **PRESIDENT’S CORPORATE CIRCLE** for their dedicated support of our mission.

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Meeting of the Minds

Groundbreaking advances aren’t made in isolation. At our unique IBD Innovate annual conference, we convene diverse stakeholders in the IBD space who are developing new products to connect, network, and learn from each other, with the goal of further accelerating the pace of novel IBD research.

The most recent IBD Innovate conference, which was held in New York City in December 2019, featured fascinating and inspiring sessions on small and large molecule drugs, precision nutrition, the gut microbiome, diagnostic tools, and medical devices, including a presentation by Maria Pereira, PhD, of Tissium, an IBD Ventures partner.

You can read more about this and other Foundation-led initiatives on the Foundation’s new blog, IBDVisible at crohnscolitisfoundation.org/blog.

CROHN’S & COLITIS FOUNDATION

Learn more at crohnscolitisfoundation.org

The Crohn’s & Colitis Foundation is the leading nonprofit 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.

Help Us Change Lives

Through your support of the Crohn’s & Colitis Foundation, you are helping to accelerate the discovery of new treatments and cures for Crohn’s and colitis, and you’re supporting those who are struggling with the physical and emotional toll of living with IBD. Help create a better tomorrow for those suffering from IBD by making a gift to the Crohn’s & Colitis Foundation today.

To make a one-time contribution to the Crohn’s & Colitis Foundation, please visit www.crohnscolitisfoundation.org/microscope.

To become a monthly donor, please visit www.crohnscolitisfoundation.org/monthly.

For additional giving options, please call 1-800-932-2423.

Leave a Legacy of Giving

You can help to strengthen the vision and commitment of the Crohn’s & Colitis Foundation by including the Foundation in your estate planning. As a member of the Founders Society you will be listed in our Annual Report, and receive inside information and updates on our research and other mission-related progress.

If you’re interested in making a planned gift or have questions regarding planned giving and the Founders Society, please contact Susan Carriker at scarriker@crohnscolitisfoundation.org.



Under the **Microscope**
GROUNDBREAKING RESEARCH AND SUPPORT FOR PEOPLE WITH IBD
CROHN’S & COLITIS FOUNDATION
SPRING 2020

Powering Innovation

A Commitment to Moving Cutting-Edge Research Forward

- Drugs that block enzymes linked to severe IBD page 4
- A super probiotic that pushes out dangerous bacteria page 5
- A revolutionary new way to treat fistulas page 5

Breaking Down Barriers

IBD Ventures is a unique venture philanthropy fund developed by the Crohn's & Colitis Foundation to fill a gap in the market by supporting the development of novel treatments, diagnostics, devices, and digital health solutions that have the potential to be game-changing for patients.

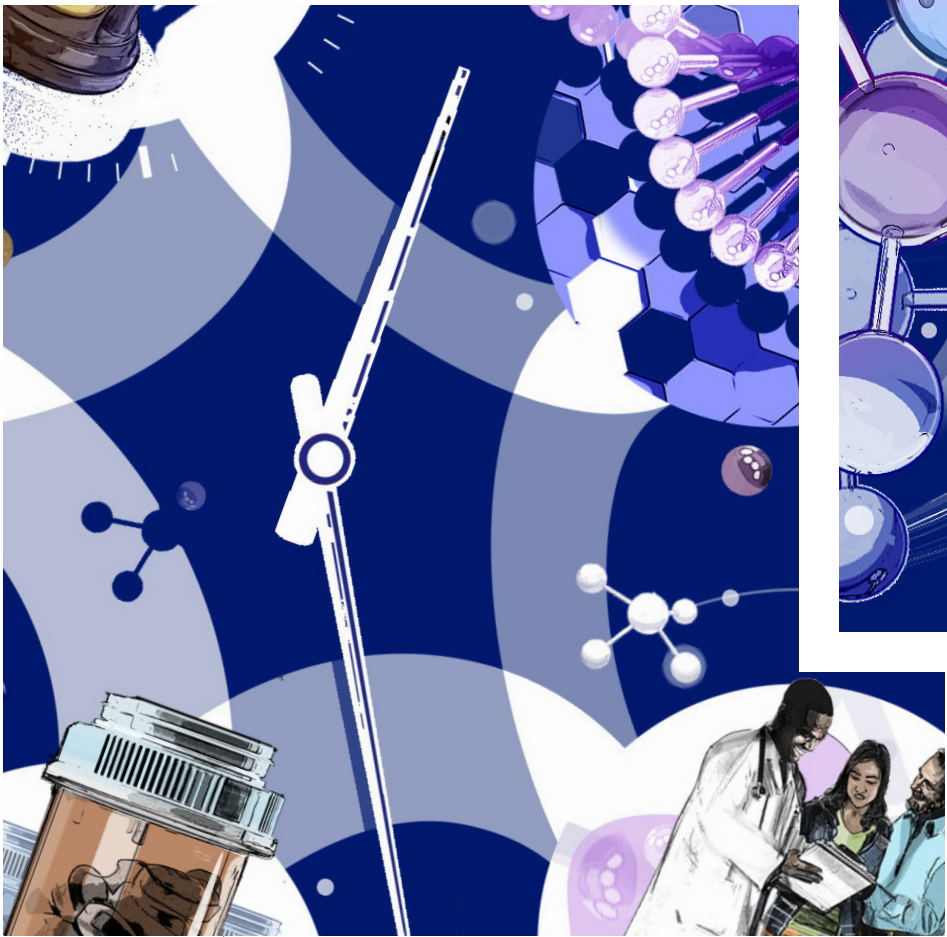
Medical breakthroughs sometimes grab media attention, but what about the stories behind the headlines? Major discoveries usually require vast investments of both time and money. The process of developing a new drug and bringing it to market, for instance, can take up to 15 years and cost more than a billion dollars. And the unfortunate reality is that many pharmaceutical companies just aren't willing to make that kind of long-term, extremely expensive investment in a very early-stage product that may or may not take off.

"Pharmaceutical companies used to fund more early-stage drug development opportunities, both in-house and also in academic labs, but most have moved away from supporting early-stage academic opportunities in favor of funding more validated, later-stage opportunities," says Caren Heller, MD, MBA, the Crohn's & Colitis Foundation's chief scientific officer.

As a result, some incredibly innovative discoveries that have great potential to help patients with inflammatory bowel disease (IBD) can get stalled indefinitely. That's where IBD Ventures comes in.

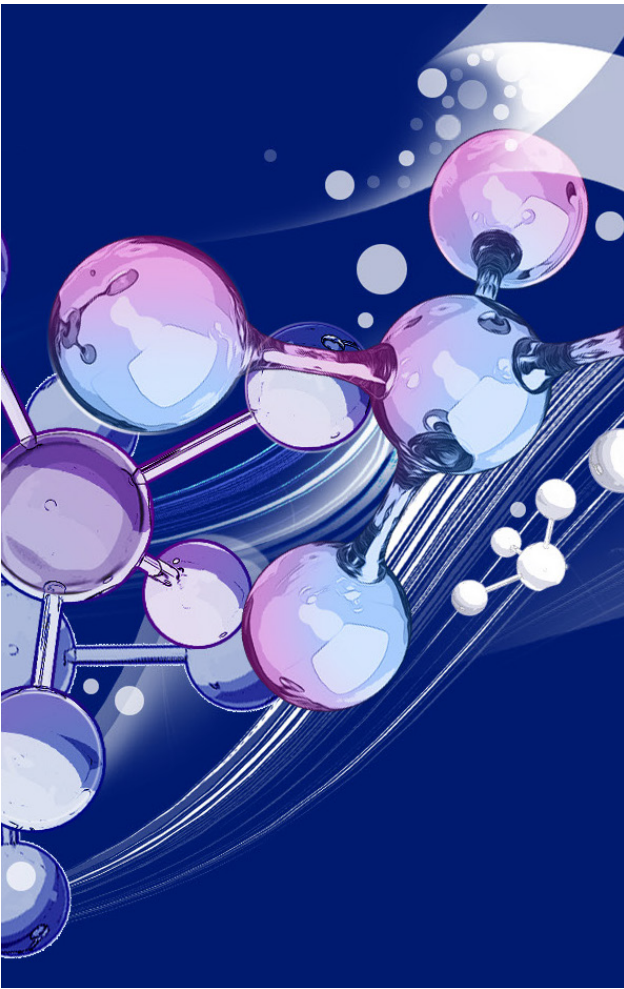
Research That Makes a Difference

IBD Ventures is the Foundation's initiative dedicated to tackling unmet patient needs by investing in early-stage research and development designed to help



bring new therapies, diagnostic tools, and medical devices to patients. As a "venture philanthropy" program, money distributed through IBD Ventures is truly being invested: If a product eventually reaches the market, the Foundation will have the ability to reinvest any financial return into additional research.

This approach enables us to foster unique collaborations between other nonprofit organizations,



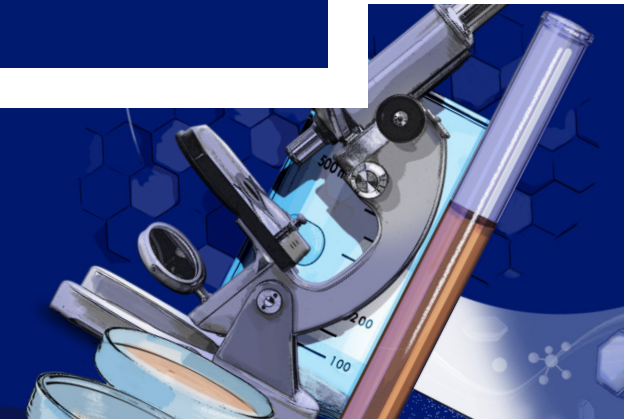
"We aim to identify the **most promising, carefully-vetted research programs** that have the greatest potential to benefit patients."

—GERARD HONIG, PHD,
the Foundation's associate director of research innovation



The Power of Potential

In order to be eligible for IBD Ventures, applicants must prove that their projects have strong potential to lead to a tangible product that would provide desperately-needed help for IBD patients. Applicants must also have a clear go-to-market strategy that leverages novel intellectual property to create a commercially viable business. In other words, you can't just have a good idea: "We're looking for a clear trajectory that can be accelerated through our support," says Honig.



academic institutions, and industries. IBD Ventures is the only investment fund exclusively dedicated to identifying and funding new product opportunities in the IBD field.

"We aim to identify the most promising, carefully-vetted research programs that have the greatest potential to benefit patients," explains Gerard Honig, PhD, the Foundation's associate director of research innovation.

IBD Ventures applications are reviewed by a volunteer committee comprised of industry and academic scientists, clinicians, and experts in biomedical entrepreneurship, along with IBD patients and caregivers.

Although IBD Ventures is relatively new—it kicked off in 2017—it has already provided funding for 11 innovative projects, nine of which are ongoing. In this issue of *Under the Microscope*, we're highlighting some of these exciting projects that we hope will lead to groundbreaking solutions for Crohn's disease and ulcerative colitis patients and bring us closer to our ultimate goal of finding cures for IBD. 🔗

Developing Novel Drug Treatments

Approximately one-third of IBD patients don't respond to the drugs that are currently on the market, and of those who do respond, many find that their initial response is not sustained and the medications eventually fail them. We need new and better options.

IBD Ventures is currently funding the development of several potential first-in-class drugs designed to block enzymes (proteins that kick-start chemical reactions) that have been associated with severe IBD and poor responses to current medications.

At the Cleveland Clinic, researchers are focusing on blocking an enzyme called PAI-1 (plasminogen activator inhibitor), which is involved in normal blood clotting. Research has already found that PAI-1 is elevated in people with severe IBD and that—at least in animal tests—inhibiting it improves the lining of the digestive tract.

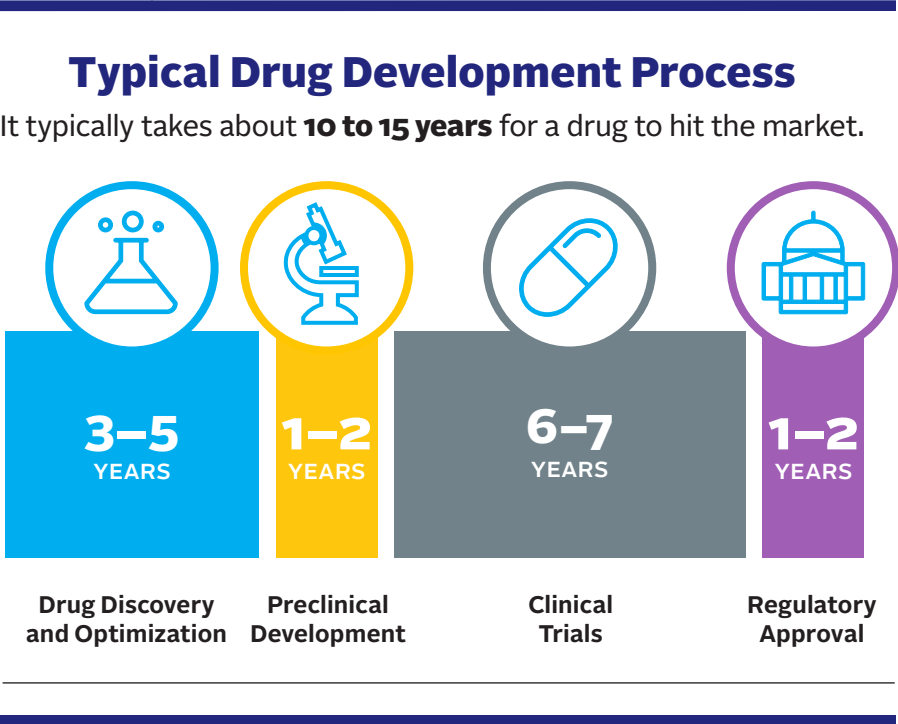
In order to advance the discovery of drug candidates capable of inhibiting PAI-1, the Foundation now provides specialized development resources for academic groups with promising new drug targets (like PAI-1) by collaborating with Evotec, a drug discovery company.

"My lab doesn't have expertise in protein production for pharmacological work; we're an academic lab," says Thad Stappenbeck, MD, PhD, who's leading the PAI-1 research at the Cleveland Clinic. "The most valuable part of partnering with IBD Ventures has been that they've paired us with people who have the right expertise." Without IBD Ventures, it would be difficult, if not impossible, to make these vital connections.

Meanwhile, at Johns Hopkins, a team of researchers led by Barbara Slusher, PhD, has been using IBD Ventures funding to further its work aimed at blocking

another enzyme, GCP11 (glutamate carboxypeptidase II), which is overactive in IBD patients. The team has already discovered a small molecule drug (which can be taken orally) that inhibits GCP11 activity in animals. They're now developing it into a formula that can be used to effectively treat humans.

"We've already proven that if you're a mouse with IBD, we can alleviate your symptoms by targeting GCP11," says Slusher. "If this works similarly [in humans], it could be used in combination with other IBD treatments or be given to patients who haven't responded to other therapies."



Without IBD Ventures, this mechanism would likely never have been explored. "There's a significant clinical need to discover new drugs for IBD because a large portion of the patients aren't served by current medications and/or have side effects that are not tolerable," adds Slusher. "I think the excitement about our enzyme inhibitor program is that it appears very well-tolerated and represents a completely novel mechanism." 🔗