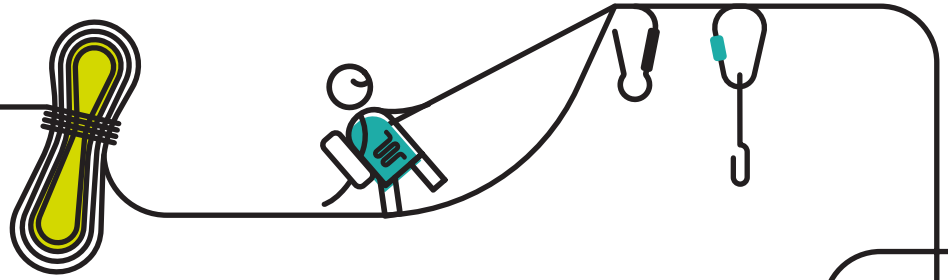
OPENBIOME

ANNUAL REPORT 2020



WELCOME

There is a touch of irony in the fact that no one saw 2020 coming. As the COVID-19 pandemic brought challenge and uncertainty to our communities, our workplaces, and our ways of life, within OpenBiome, our focus remained clear.

Safe access to fecal microbiota transplantation (FMT) matters deeply to the thousands of patients with intractable *C. difficile* infections who need it each year. As the only national stool bank, OpenBiome's work to enable this access provides unique and critical support to patients, their loved ones, and the healthcare community working to restore people's well-being. Beyond this immediate impact, our work to catalyze research on the human microbiome is spurring an emerging field of microbiome-based medicine. For future patients, these new discoveries offer a path to remedy some of the largest unmet needs in public health.

As we continue in our efforts to support the exploration of this new field, and scale it to new heights, 2020 and the threats posed by the COVID-19 pandemic presented some of the biggest challenges to this work in our seven-year history. It was this clearsighted focus on the promise that FMT holds for so many people that drove our efforts to deliver on our mission.

As one patient shared:

> "I contracted C. diff at the beginning of the COVID-19 pandemic, and I suffered for so long. Not a single antibiotic treatment worked. I was in and out of the hospital constantly. For a time, I was absolutely hopeless, but then I was approved for an FMT. Not only did the donor's stool donation improve my life, but their actions caused a ripple effect for good. By receiving an FMT and getting my life back, I was able to once again contribute and better the lives of the children and adolescents I work with."

The impact of offering safe access to FMT is felt beyond the patients who receive the treatment they need. Enabling safe access to FMT also depends on more than OpenBiome's efforts alone. As this year highlighted so poignantly, maintaining public health takes the commitment and care of the healthcare professionals, scientists, public health officials, advocates, and so many others working in concert towards the objective of supporting safe, reliable care. Together, our collective impact is felt not only by those who are restored to health, but also by their friends and loved ones, and all those who they touch in their broader communities.

To those who shared in this work, thank you for being a ripple effect for good. This year, of all years, the impact was, as they say, unprecedented.

CAROLYN EDELSTEIN
EXECUTIVE DIRECTOR

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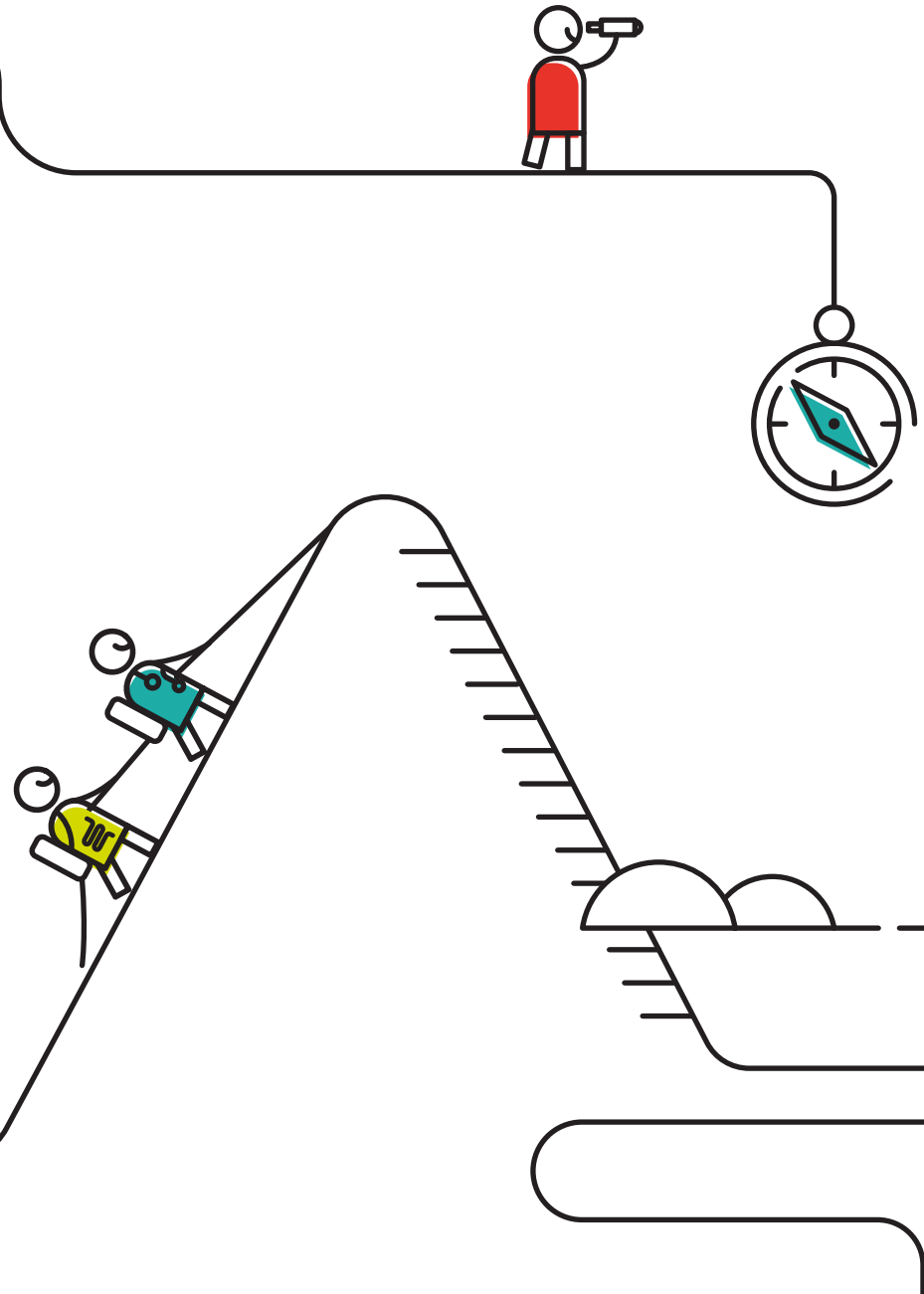


TREATING PATIENTS

In 2020, OpenBiome and our clinical network adapted our practices to continue serving patients with recurrent *C. difficile* infection (rCDI) during the COVID-19 pandemic.

To maintain access to Fecal Microbiota Transplantation (FMT), we addressed the risk that SARS-CoV-2 (the virus that causes COVID-19) could potentially be transmitted through stool. This involved relying both on our existing operations—such as our pharmacovigilance program, which tracks the health outcomes of FMT recipients—and building new systems and capacity.

Using our experience with driving advancements in donor screening and responding to new health risks, we implemented SARS-CoV-2 testing via nasopharyngeal swabs and worked closely with a microbiome informatics company to develop a direct stool test for the virus.

We also shared our knowledge and contributed to discussions among the FMT community by publishing a mathematical tool for evaluating donor screening strategies.

Every treatment counts

In 2020, OpenBiome shipped out **3,445** FMT treatments to our clinical network comprising more than 1,250 hospitals and clinics across the Unites States. Many of these treatments were used to serve emergency cases where patients had severe *C. difficile* infections. Since 2013, we have shipped **56,906** FMT units to our clinical partners.

Answering a Pressing Clinical Question

To help evaluate screening strategies testing stool donors for SARS-CoV-2, OpenBiome published a mathematical model in the academic journal "Open Forum Infectious Diseases."

In their own words:

"After six hospital visits, we said enough is enough...[My wife] checked into a Medical Center for the procedure. It was successful. We are so grateful after 3 years of doing battle. I am 84 years young and my wife, who is younger and faster, is 80. God bless you for all you have done."

- JOHN AND LINDA

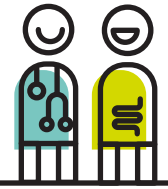
Answering a Pressing Clinical Question

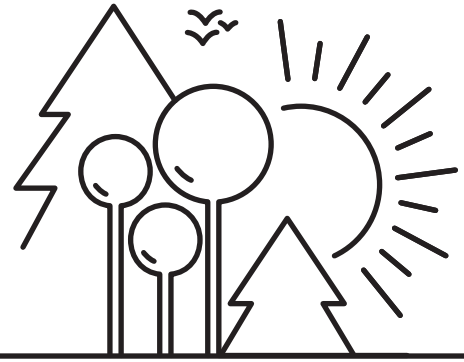
To help evaluate screening strategies testing stool donors for SARS-CoV-2, OpenBiome published a mathematical model in the academic journal "Open Forum Infectious Diseases."

"One of the most critical issues for stool banks during the pandemic was how to screen donors for SARS-CoV-2 and prevent possible transmission through FMT to patients. To help answer this question, we built a model of FMT donors—simulating their donation schedule, SARS-COV-2 infection incidence, and COVID-19 disease course. On top of this, we incorporated various screening strategies accounting for the imperfect specificity and sensitivity of each test. As the pandemic and knowledge of SARS-CoV-2 evolved, this model served as a guide for designing an effective screening protocol."

- SCOTT OLESEN

PhD. Scientific Director of OpenBiome and Lead Author of "Modeling Donor Screening Strategies to Reduce the Risk of Severe Acute Respiratory Syndrome Coronavirus 2 Transmission via Fecal Microbiota Transplantation."





PATIENT SAFETY

As OpenBiome monitored the spread of SARS-CoV-2, we paid close attention to emerging research suggesting that the virus can be shed[1] and therefore potentially transmitted via stool[2] from both COVID-19 symptomatic and asymptomatic individuals. To date, the infectivity of viral particles is not yet known and there have been no reports of SARS-CoV-2 transmission by FMT. We nonetheless took action to mitigate this potential risk:

Protecting Patients

To protect FMT recipients from potential transmission of SARS-CoV-2, OpenBiome adopted new safety policies including:

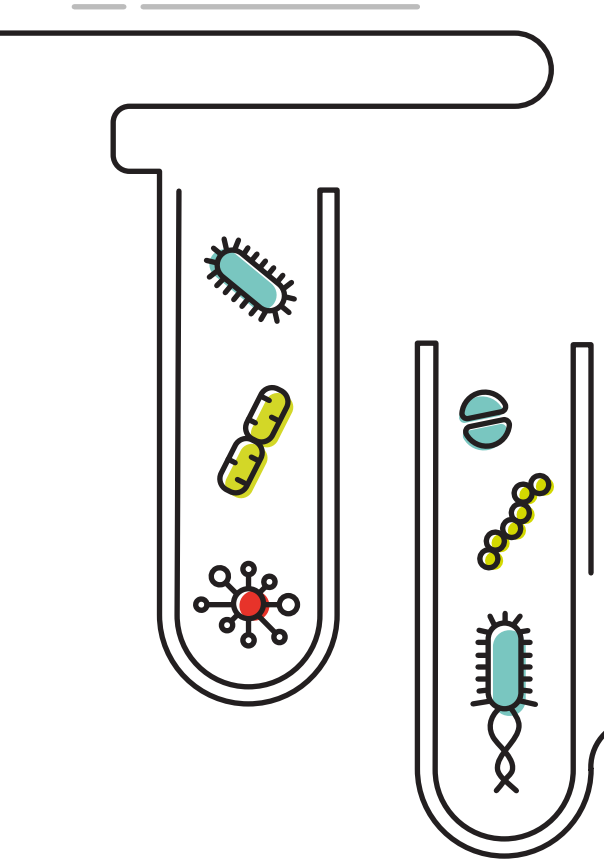
- Only providing FMT material that was processed before December 1, 2019, in line with FDA guidance.
- Quarantining material processed after December 1, 2019 until we could use a direct stool test to screen for SARS-CoV-2.
- Proactively implementing new donor screening for SARS-COV-2 that included molecular testing via nasopharyngeal swabs as well as screening for COVID-19 risk factors and symptoms.
- Driving and implementing a new method for directly testing for SARS-CoV-2 in stool.

Updating Best Practices

During this time of uncertainty and rapidly evolving information, OpenBiome helped the medical community stay up-to-date and implement best practices for FMT by sharing guidance from the FDA, medical societies, and our clinical staff. We provided information on:

- The risk of transmitting SARS-CoV-2 through stool.
- Minimizing SARS-CoV-2 exposure while performing FMT.
- Planning for urgent, time-sensitive cases.
- Using our capsule formulation as a non-aerosol-generating alternative to the delivery of liquid FMT via the upper or lower GI tract.

Additionally, several of our clinical partners participated in an international expert panel on screening stool donors and reorganizing FMT services during the COVID-19 pandemic.



[1] Xiao, F., Tang, M., Zheng, X., Liu, Y., Li, X., & Shan, H. (2020). Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology, 158(6), 1831-1833.e3. doi: 10.1053/j.gastro.2020.02.055 [2] Gu, J., Han, B., & Wang, J. (2020). COVID-19: Gastrointestinal Manifestations and Potential Fecal–Oral Transmission. Gastroenterology, 158(6), 1518-1519. doi: 10.1053/j.gastro.2020.02.054

Developing a New Test

Protecting FMT recipients from SARS-CoV-2 required building new screening capabilities. While we could screen stool donors using genetic testing via nasopharyngeal swabs, there was no test that could directly detect the virus in processed stool samples.

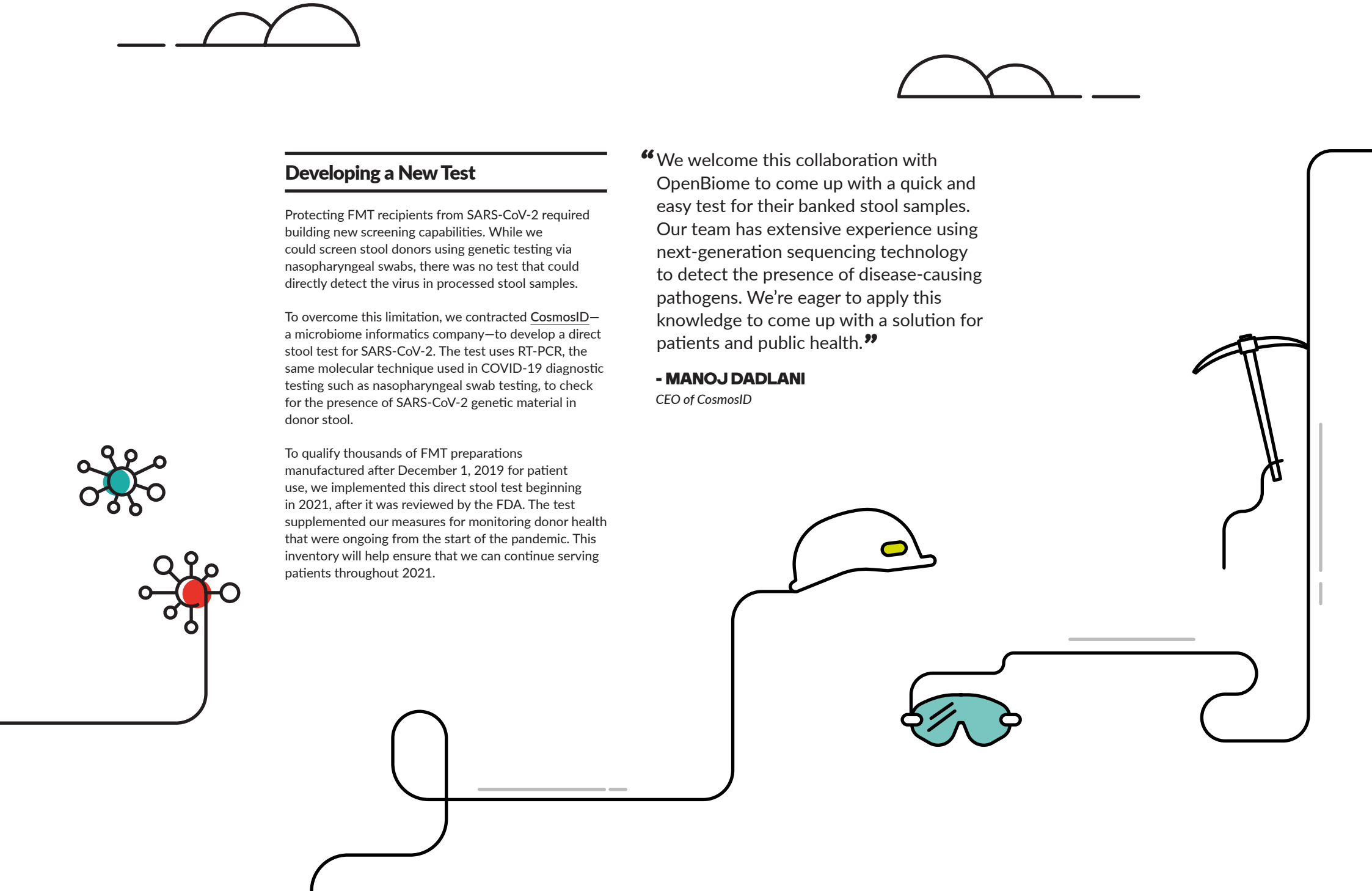
To overcome this limitation, we contracted CosmosID—a microbiome informatics company—to develop a direct stool test for SARS-CoV-2. The test uses RT-PCR, the same molecular technique used in COVID-19 diagnostic testing such as nasopharyngeal swab testing, to check for the presence of SARS-CoV-2 genetic material in donor stool.

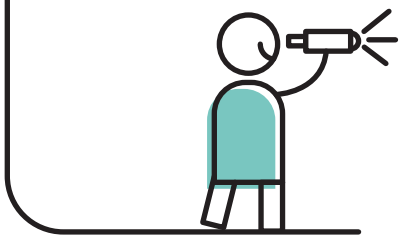
To qualify thousands of FMT preparations manufactured after December 1, 2019 for patient use, we implemented this direct stool test beginning in 2021, after it was reviewed by the FDA. The test supplemented our measures for monitoring donor health that were ongoing from the start of the pandemic. This inventory will help ensure that we can continue serving patients throughout 2021.

> “We welcome this collaboration with OpenBiome to come up with a quick and easy test for their banked stool samples. Our team has extensive experience using next-generation sequencing technology to detect the presence of disease-causing pathogens. We’re eager to apply this knowledge to come up with a solution for patients and public health.”

- MANOJ DADLANI

CEO of CosmosID





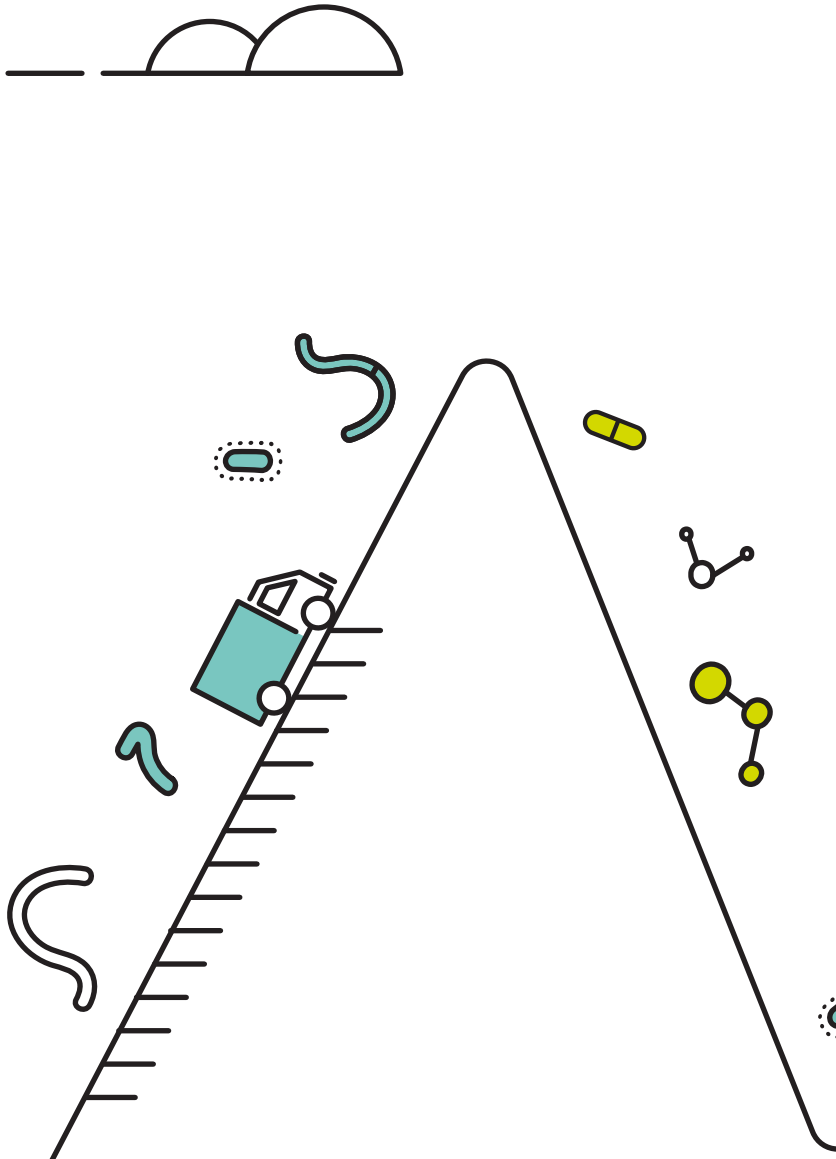
A BRIDGE TO THE FUTURE

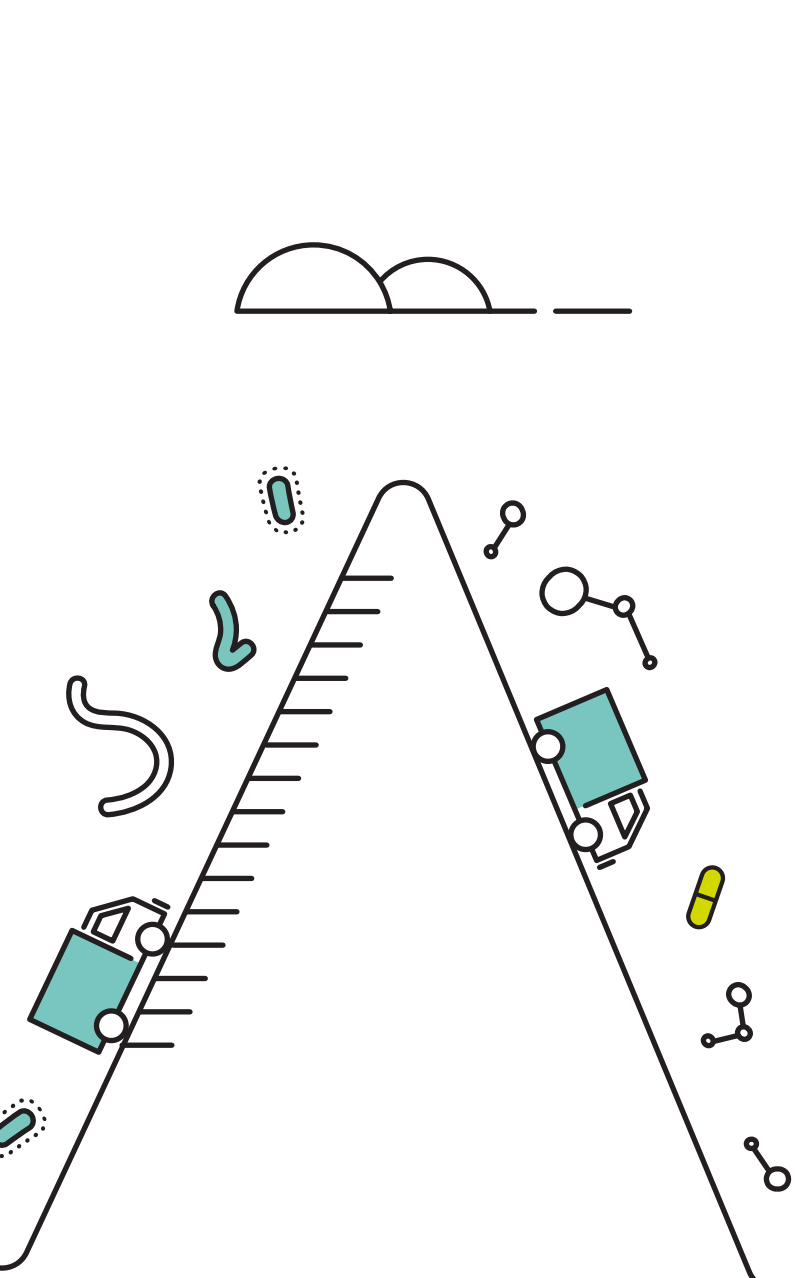
OpenBiome was founded to provide an immediate solution to an urgent healthcare need—treating patients with recurrent *C. difficile* infection (rCDI) who have failed standard antibiotic regimens. For these patients, an FMT is often a last resort to recover from a debilitating infection.

Despite its promise, FMT is still an investigational treatment. It is available to patients outside of clinical trials through a policy that the FDA put in place in 2013. As a result of this status, many patients have gained access to treatment, but patients still experience difficulties, including limitations on insurance coverage, and many physicians face challenges bringing an FMT program to their hospitals.

In the long run, we believe that an FDA-approved microbiome-based therapy for rCDI that has demonstrated safety and efficacy in well-controlled clinical trials is the best treatment option for patients.

During the summer of 2020, biopharmaceutical companies announced positive results from three separate pivotal trials showing safety and efficacy of microbiome-based treatments to prevent recurrent *C. difficile* infection. These exciting data suggest that an FDA-approved alternative to FMT will be available to patients in the next few years. Until that time, OpenBiome is committed to bridging care for patients as they wait for the potential of this new field of medicine to be realized.

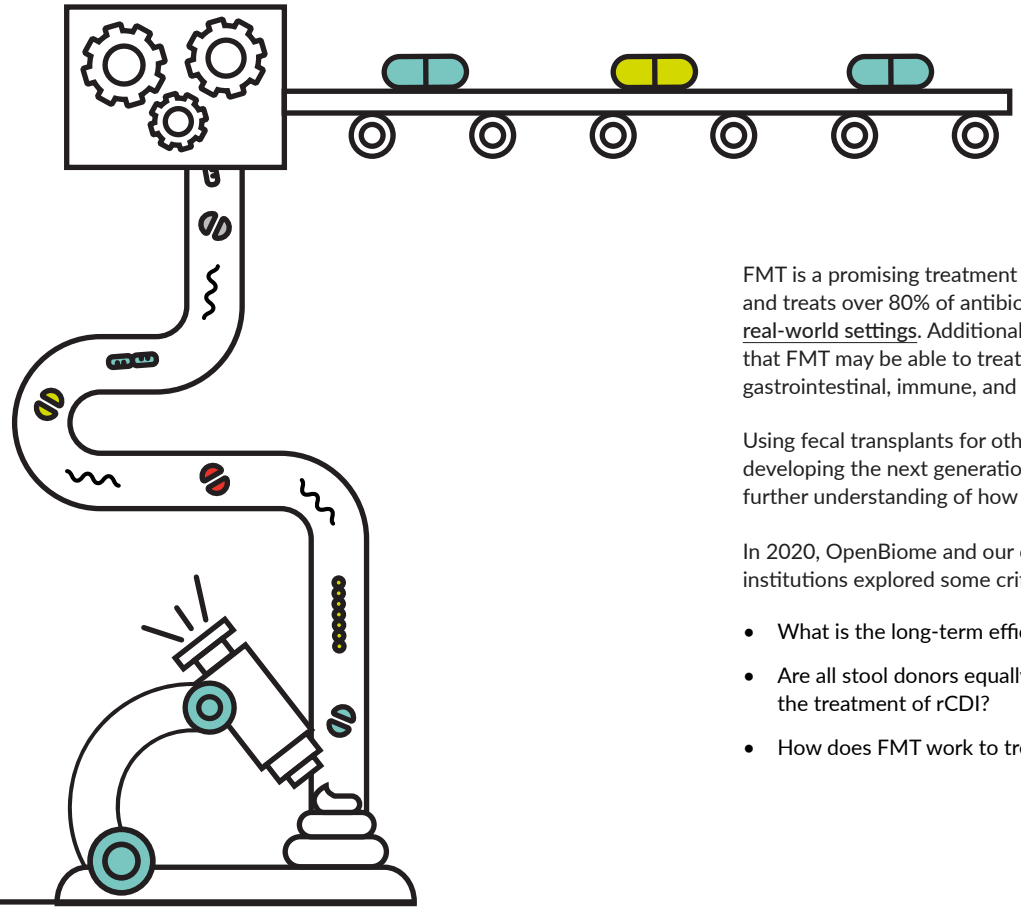




> “The microbiome-based therapeutics in development represent the cutting edge of a new field of medicine. FDA approval of these products would improve patient care and help open the doors to new clinical applications for FMT to advance public health. In the future, we hope to see microbiome-based treatments for many other indications beyond *C. difficile* infection.”

-DR. MAJDI OSMAN

MD MPH. Chief Medical Officer of Openbiome



CATALYZING RESEARCH

FMT is a promising treatment for recurrent *C. difficile* infections (rCDI) and treats over 80% of antibiotic-resistant cases in clinical trials and real-world settings. Additionally, a growing body of evidence suggests that FMT may be able to treat a wide range of illnesses including gastrointestinal, immune, and neuropsychological disorders.

Using fecal transplants for other indications beyond rCDI and developing the next generation of microbiome-based therapies requires further understanding of how FMT affects the body.

In 2020, OpenBiome and our collaborators at academic research institutions explored some critical questions including:

- What is the long-term efficacy and safety of FMT for rCDI?
- Are all stool donors equally effective at providing FMT material for the treatment of rCDI?
- How does FMT work to treat rCDI on a molecular and cellular level?

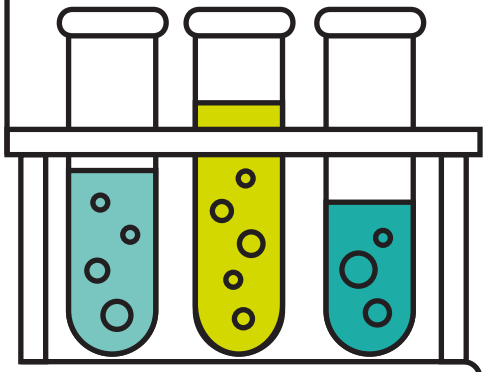
Selected Publications

Long-term effects and safety of fecal microbiota transplantation for treatment of recurrent Clostridioides difficile infection (Journal Of Clinical Gastroenterology)

While several clinical trials have described the short-term efficacy and safety for FMT, the microbiome field is still gathering data on the long-term effects of fecal transplants. This study, the largest and longest of its kind to date, tracked patients for 6 to 84 months after their fecal transplants. Researchers found that most participants experienced long-term cure, with no signs of long-term health risks.

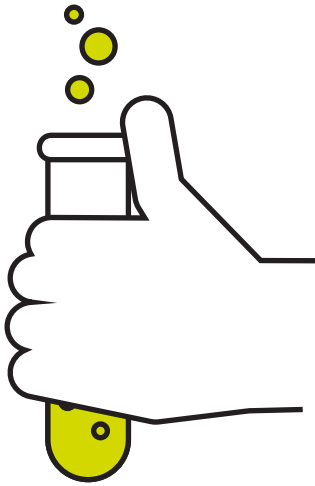
Fecal microbiota transplantation "donor effects" are not clinically relevant for Clostridioides difficile infection (Gastroenterology)

Researchers have speculated whether strategies to match stool donors to patients based on gender, ethnicity, the presence of particular gut bacteria or metabolites, and other factors could improve the efficacy of FMT. This study, analyzing 6,053 patients treated with FMT material provided by 249 OpenBiome donors, found that such potential "donor effects" were not a relevant factor in CDI patient care, and that stool from a screened donor is suitable to treat any patient with CDI.

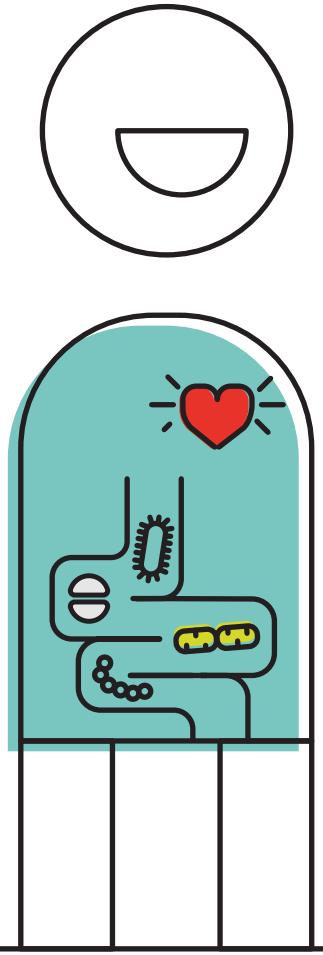


Understanding the mechanisms of efficacy of fecal microbiota transplant in treating recurrent Clostridioides difficile infection and beyond: the contribution of gut microbial-derived metabolites (Gut Microbes)

Once in the patient's digestive tract, bacteria from a stool donor produce a batch of molecules such as metabolites and signaling factors. This paper describes which of these molecules may play a key role in patient recovery. Using this knowledge, researchers are working to engineer more defined therapies that transplant a consortium of rationally selected bacteria rather than an entire microbiome.



RESEARCH SPOTLIGHTS



OpenBiome is working with leading academic researchers to build a new relationship between microbes and healthcare. Instead of viewing bacteria as pathogens to be eradicated, we are exploring whether microbiome-based therapies can prevent or remedy some of the most common and difficult-to-treat illnesses.

Our clinical trials portfolio, reflecting the broad therapeutic potential of FMT, spans autoimmune, infectious, metabolic, and neuropsychiatric diseases.

15 Clinical Trials and SPINDs

In 2020, OpenBiome supported 12 clinical trials by providing FMT preparations along with guidance on trial design, safety review, and regulatory consultation. Our normal operations were largely suspended as hospitals and research facilities paused enrollment in order to help combat the COVID-19 pandemic. Most of our work with clinical researchers occurred before the pandemic affected the United States or later in the year when it was safe and appropriate to resume trials.

In addition to clinical trials, we supported 3 Single Patient Investigational New Drug Applications (IND)--an expanded access program run by the FDA that allows doctors to use unapproved treatments for patients with serious or life-threatening conditions.

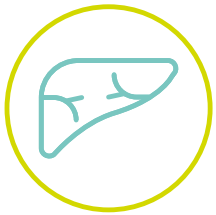
Selected Publications

OpenBiome and our research collaborators published 35 academic papers in peer-reviewed journals such as The Lancet Gastroenterology & Hepatology, The Journal of the American Medical Association (JAMA), and Gastroenterology. Two studies are spotlighted below.

Antibiotic-Resistant Infection in Patients with Cirrhosis

Patients with cirrhosis—a late-stage liver disease where healthy tissue is replaced by scar tissue—are especially vulnerable to antibiotic-resistant infections. For these patients, an infection can be dire, bringing on liver failure, delisting from the liver transplant list, and death.

Working together on a Phase 1 Clinical Trial, OpenBiome and researchers from Virginia Commonwealth University, demonstrated that FMT can help protect patients. Fecal transplants, delivered by capsule or enema, decreased the activity of antibiotic-resistant genes that make infections difficult to treat. The results of the trial were published in Hepatology Communications and provide the foundation for follow-up studies.



Immune Checkpoint Inhibitor Colitis (ICI Colitis)

Immune checkpoint inhibitors are powerful anti-cancer drugs that boost immune response to cancer cells but can also cause colitis or dangerous inflammation of the colon.

Physicians from Roswell Park Comprehensive Cancer Center in Buffalo, New York used OpenBiome material to treat a case of ICI Colitis not responding to standard steroid regimens. The patient, a 71-year-old man, was experiencing severe diarrhea and required IV narcotics for pain control. These symptoms abated ten days after his FMT and he was able to return home from the hospital.

A case study of this patient, just the second report on FMT in the management of ICI colitis, was published in The American College of Gastroenterology Case Reports Journal and is helping drive further research on this new application of fecal transplants. The use of FMT in this case was provided under a single patient investigational new drug application (SPIND), an FDA program that grants patients with serious or life-threatening conditions expanded access to unapproved therapies.

ABOUT US

OpenBiome's mission is to expand safe access to fecal microbiota transplantation for patients with recurrent *C. difficile* infection and to catalyze research on the human microbiome.

Founded in 2012 at MIT, OpenBiome aims to reduce the practical barriers to providing FMT and enable translational research investigating new applications of microbiome-based therapies.

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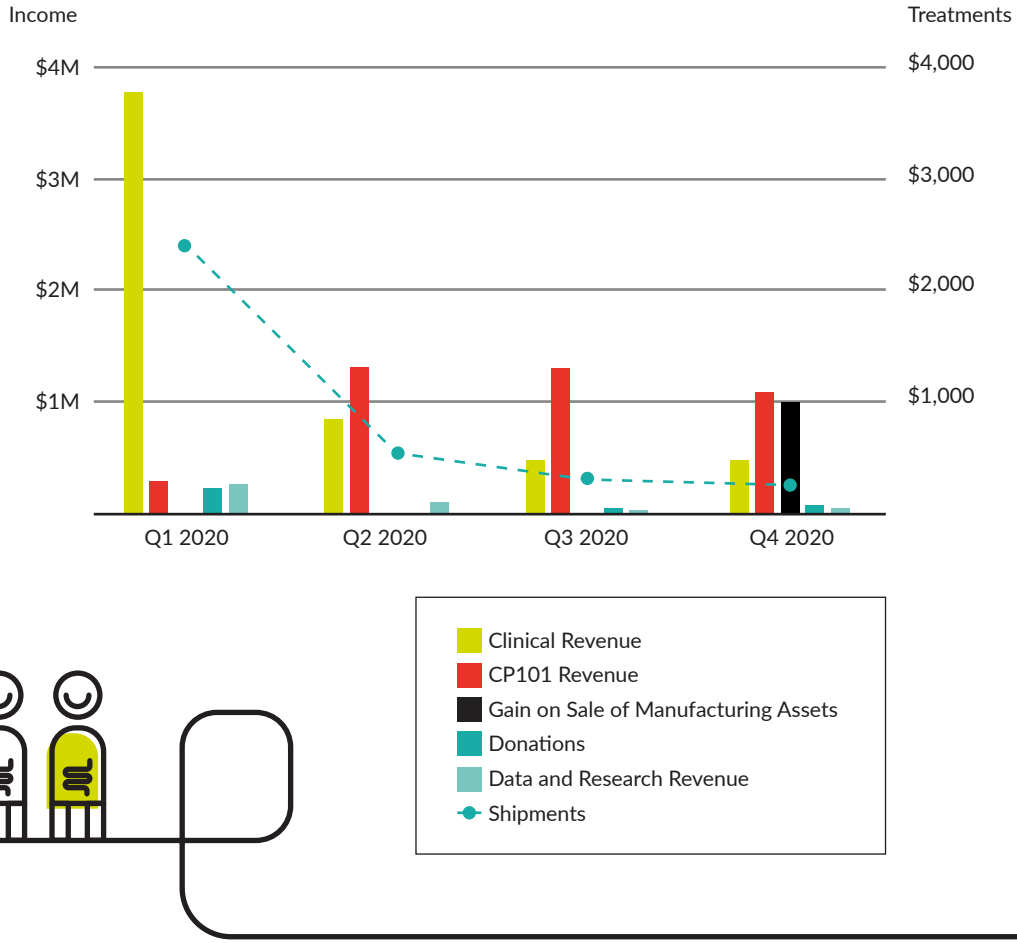
FINANCIALS

2020 Quarterly Revenue



Balance Sheet

Assets

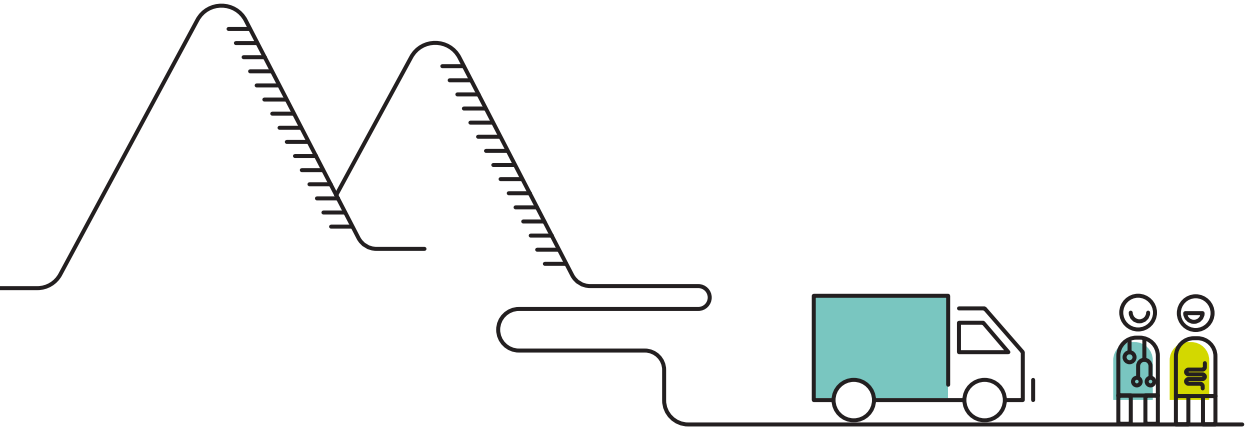
Current Assets	2020	2019
Cash and equivalents	$2,514,362	$4,460,778
Accounts receivable, net	$291,501	$2,114,339
Inventory, net	$4,625,678	$3,763,989
Net accounts receivable - related party	$180,937	-
Prepaid expenses	$171,964	$163,297
Total current assets	$7,784,442	$10,502,403
Property and equipment, net	$410,995	$757,581
Security deposits	$62,055	$84,782
Total assets	$8,257,492	$11,344,766

Liabilities and Net Assets

Current liabilities		
Accounts payable	$220,734	$567,387
Net accounts payable - related party	-	$3,259,488
Accrued expenses	$500,354	$178,965
Current portion of Paycheck Protection Program Loan	$385,078	-
Deferred revenue	$22,100	$17,790
Total current liabilities	$1,128,266	$4,023,630
Paycheck Protection Program Loan	$770,239	-
Total liabilities	$1,898,505	$4,023,630
Net assets		
Without donor restrictions	$6,358,987	$7,215,813
With donor restrictions	-	$105,323
Total net assets	$6,358,987	$7,321,136
Total liabilities and net assets	$8,257,492	$11,344,766

Income Statement

	2020			2019
	Without Donor Restrictions	With Donor Restrictions	Total	Total Without Donor Restrictions
Operating revenues and support				
Sales of product (net of discounts)	$5,256,585	-	$5,256,585	$14,139,523
CP101 revenue	$4,022,826		$4,022,826	-
Research activities:				
Contact revenue	$88,544	-	$88,544	$227,482
General research revenue	-	-	-	$52,525
Grant revenue	$76,000	-	$76,000	$373,277
Shipping and handling fees	$278,520	-	$278,520	$694,550
Less cost of clinical program sales	($7,043,384)	-	($7,043,384)	($5,224,052)
Gross profit on sales	$2,679,091	-	$2,679,091	$10,263,305
Data licenses and royalties	$220,000	-	$220,000	$220,000
Other income	$39,796	-	$39,796	$21,570
Other donations	$287,967	-	$287,967	$37,314
Release from restrictions	$105,323	($105,323)	-	-
Total operating revenues & support	$3,332,177	($105,323)	$3,226,854	$10,542,189
Operating expenses:				
Program:				
Clinical	$2,955,269	-	$2,955,269	$3,266,448
Research	$1,694,361	-	$1,694,361	$2,091,052
Total program expenses	$4,649,630	-	$4,649,630	$5,357,500
General and administrative	$489,122	-	$489,122	$609,232
Fundraising	$50,251	-	$50,251	$141,716
Total operating expenses	$5,189,003	-	$5,189,003	$6,108,448
Change in net assets from operations	($1,856,826)	($105,323)	($1,962,149)	$4,433,741
Non-operating activities:				
Gain on sale of assets (Note XX)	$1,000,000	-	$1,000,000	-
Change in net assets	($856,826)	($105,323)	($962,149)	$4,433,741
Net assets, beginning of year	$7,215,813	$105,323	$7,321,136	$2,887,395
Net assets, end of year	$6,358,987	-	$6,358,987	$7,321,136



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2067 Massachusetts Ave, Cambridge MA 02140