Slice of MIT Podcast | Gross Science: Fecal Transplants and the Microbiome

HOST: This episode comes with our first ever disclaimer. In this episode, we talk about what we call gross science. We're going to talk a lot about bodily functions and the workings of the digestive system. If you're squeamish, this episode might not be for you.

[SLICE OF MIT THEME MUSIC]

ANNOUNCER: You're listening to the *Slice of MIT* podcast, a production of the MIT Alumni Association.

HOST: Mark Smith is walking me through his lab, and it looks like your typical lab. It has a processing area, some fridges, lots of pipettes, and is impeccably clean. It seems standard so far, right? That is until Mark explains the purpose of the air jets that you can hear clicking on and off.

MARK SMITH: So the biosafety cabinet is setup to protect us from the poo and the poo from us. And so there is basically some sophisticated air jets that protects--

HOST: Yes, you heard that right. Mark just said poop. Mark is the research director and co-founder of OpenBiome, a nonprofit stool bank that works to expand safe access to fecal transplants. Currently, fecal transplants are used as a treatment for people suffering from Clostridium difficile, commonly known as C diff. OpenBiome is the only stool bank of its kind and is operating to connect donors and C diff patients as well as get a better understanding of our microbiome. That's the community of bacteria inside each one of us.

In this episode of the *Slice of MIT* podcast, we'll learn how Mark transitioned from researching the microbiome at MIT to co-founding a stool bank. Mark tells us how a stool sample makes the journey from donor to patient. And he'll share a little bit about Open Biome's process for keeping donor identities a secret.

SMITH: We have a whole range. I think my personal favorite was Vladamir Putin.

HOST: Stay tuned.

[MUSIC PLAYING]

Mark graduated from Princeton with a degree in biology and enrolled at MIT to pursue his PhD in biology and biological engineering. He had an interest in the microbiome and was an active researcher in the Alm lab led by PI Eric Alm. The lab develops complementary, computational,

and experimental methods to engineer the human microbiome.

It was during his time at MIT that Mark found out that a friend had C diff, a nasty infection that causes severe diarrhea and a whole host of other problems. The infection is usually the result of antibiotic use for an unrelated illness, and around half a million Americans are affected by C diff each year.

SMITH: He went into his gallbladder removed. He came home without his gallbladder but with C diff. It went on antibiotics postoperative. When he went off the antibiotics he was very sick with C diff.

HOST: This friend went through seven rounds of vancomycin therapy, an antibiotic used to treat bacterial infections. The treatments failed each time, leaving him sick for over a year. So the friend began exploring other options.

SMITH: There's one doctor in New York City that offer fecal transplants at the time, and he was going to have to wait for six months to get treatment from that guy. So it's a very, very long crazy process. So he ended up doing it at home with his roommate's stool in an apartment in New York with a blender and at home enema kit. And it worked for him, but it was just really crazy to see that whole process.

HOST: Now, we're definitely not recommending performing fecal transplants at home by getting a stool donation from a friend, but the process isn't unheard of. Fecal transplants have been shown to be 90% effective in treating recurring C diff, meaning the transplants are effective, but, unfortunately, aren't readily available. That is until Mark co-founded OpenBiome.

The name OpenBiome is a spin on microbiome. If you've never heard of the microbiome until this podcast, you're not alone. The concept of the microbiome and the idea that the bacteria in our body work as a community is fairly new, something scientists only began seriously researching within the past few decades. Mark is able to explain the microbiome and how C diff messes with it in a way that just about anyone can understand.

SMITH: We know that antibiotic exposure is actually the primary risk factor for developing C diff. Think about your microbiome as like this rain forest, so it's this very complex community. And then you take antibiotics, and that's like coming in and clear-cutting the rain forest, cutting everything down, burning it down, so there's not too much left. And then you can see, it's just like this weed that comes in, and it recolonizes the environment before the rest of the other bacteria can come back in. And its strategy is it knows that the other bacteria are going to out

compete it if they have the opportunity to. So what they do is it produces these toxins that actually induce really severe diarrhea in the host. And from the bacteria's perspective, it's really great because it prevents the other guys from coming in that might out compete it.

HOST: Mark says that C diff likes to colonize by leaving spores in your large intestine.

SMITH: So what you're doing when you treat these patients with antibiotics, your hoping that, while they're on antibiotics, you'll basically wash out all the spores and that you'll treat them with antibiotics long enough. And then they'll get naturally recolonized with other bacteria before the C diff comes back. And it does work. Like At least in first onset disease, antibiotics are reasonably effective. Only about 20% of patients will end up with a recurrence. But once you have a recurrence, then you've already eliminated whatever was left of the microbiome that would normally out compete C diff. And now you're probability of getting a second recurrence is much higher. So 20% on first onset disease, then it's 40%, and then it's 60%. And then there's this core of patients that are really in trouble, who just don't respond really well to any therapy.

HOST: That's where fecal transplants come in. A fecal transplant works like this. A healthy person donates their stool to a place like OpenBiome. The stool is then processed and transplanted by way of an enema to a patient who is suffering from C diff. The fecal transplant introduces healthy bacteria to the C diff patient. And in 90% of the cases, the recurrent C diff infection is cured.

SMITH: We have something that's very simple, very inexpensive, very, very effective. And yet, there are patients that need it and don't have access to it. Part of it was, I think at the time, it was very time-intensive for doctors to be able to offer the procedure because they would need to do this intensive screening process. It has all this coordination involved, and it's a very long process.

HOST: OpenBiome worked to standardize that intensive process and has been providing safe access to fecal transplants since 2012. So what does that look like? Well first, you start with the donors.

SMITH: Less than 3% of prospective donors end up getting enrolled as qualified donors. It's harder to be a donor than it is to get into MIT.

HOST: In order to be a stool bank donor, you must be generally healthy and pass numerous tests.

SMITH: So you have your standard set of questions that are used for blood banks plus a lot more. Because we don't know what the risk factors might be, so we try to be as comprehensive as possible. Because in the absence of evidence, we want to always make the most conservative decision that we can.

HOST: Donor stool samples and blood samples are then sent out for testing for infectious diseases and bacterial and viral infections. If these samples pass, the donors can enroll. Because of this lengthy process, OpenBiome tries hard to hold onto their donors.

SMITH: The idea is we've invested quite a bit in finding them. So we like to come in as often as possible. So we try to set it up so there are donors coming in on a daily basis or near daily basis.

HOST: Some donors drop off samples multiple times per day.

SMITH: We'll randomly test them actually during the window, and then at the end we'll do another testing round.

HOST: Safety is obviously a big priority for OpenBiome, but so is anonymity. That's why Mark and his team employ a unique naming convention to keep their donor's identities a secret.

SMITH: We have a whole range. I think my personal favorite was Vladimir Pootin. He's a retired donor. We're always taking suggestions for new names if you have any good ideas. But we've got a fairly long list of potential donor nicknames.

HOST: When an approved donor sample comes in, say from someone like Vladimir Pootin or Albutt Einstein, they're dropped off at OpenBiome's Medford lab. Samples are transferred from donor to lab in what looks like a Cool Whip container. After the samples make it to the lab, the fun starts. Mark shows me how they transform a fecal donation into a usable transplant for a C diff patient.

SMITH: The process is fairly simple. We'll take that container with stool in it. We'll put it in basically a bag, and it's got a filter in it. And the sample will go on one side of the bag. And then we'll add in-- so we have a buffer saline glycerol here. It goes through a filter to sterilize it. We'll pump in an appropriate volume for the size of the sample. So based on how big the poop sample is we'll have more or less buffer So we'll add in the liquid. We'll seal up this bag. There's a cuff that goes on it. Then we put it over into this thing which is called the jumbo mix.

HOST: This jumbo mix is essentially a punching machine with metal paddles walloping the sample. You can see basically it smushes up the poop into the liquid. So you've got this liquid slurry. And the fibrous material stays on this side of the bag. And there's this 330 micron filter and all the liquid can pass through the filter. And we'll use some serological pipette to basically pull off the liquid from one side. And then we'll distribute it into the treatment bottles, which are in these guys. And that liquid slurry that comes off is what actually goes into patients.

SMITH: The reason we filter it is when it's being delivered to patients it has to fit through a very narrow tube. And if that tube gets clogged up with poop, it's very bad for everybody, as you might imagine. For each sample we save a safety aliquot that we can go back to in case there's an adverse event. So we go back and do an investigation on the specific sample that went into patient. And we save additional samples for research. So we have some collaborations with MIT. We'll do some sequencing and analysis. But then other than that, we take the bottles when they're full. And then we bring them back out here.

HOST: To a separate part of the lab with a massive freezer.

SMITH: And pop them in a minus 80 freezer. And within this you can see neatly stacked rows of bottles of poop.

HOST: These bottles look just like little plastic juice bottles, except for their color, which is, of course, brown.

SMITH: And then their material stays in quarantine for 60 days until we've been able to screen it for a second time. So you know they're healthy in the beginning. We know they're healthy at the end.

HOST: The samples are then shipped off to over 350 hospitals to be used by their patients. This streamlined process has allowed thousands of C diff patients to have access to treatment. Currently, OpenBiome only produces fecal transplants for treating C diff. But part of OpenBiome's operations include research on our guts and other uses for fecal transplants. Mark and OpenBiome work regularly with the Center for Microbiome Informatics and Therapeutics, a collaboration between MIT and Mass General Hospital, and also help to support other research by funding pro-bono treatments and supporting clinical and transitional research studies.

SMITH: For C diff all the donors behave the same. But for some of these other diseases, it looks like

there are some donors that behave better than others. And so trying to figure out what's going on with that is interesting. And we're working on developing a process for long-term maintenance therapy. So not just a single intervention-- we have oral capsules that you can take. So you just swallow a pill with poop in it basically. And the idea is that that enables long-term maintenance therapies.

HOST: Meaning patients can have more consistent control of their microbiome rather than seeking treatment only when things are really bad. OpenBiome's patient count continues to grow.

SMITH: I think our view is we set up OpenBiome to treat C diff and to make sure that patients have access to that, and we've achieved a lot of our goals there. I mean, our first year we treated six patients. We wanted to treat 1,000 in the second year, and we treated 2000 in the second year. And then this year our goal was to treat 10% of all recurrent C diff in this country by the end of the year, and we're already about there. So a lot of ways, I feel like most of the recurrent C diff patients that really need this have access or will soon have access to this. And now the next big thing for us is finding other diseases that we might be able to have an impact on.

HOST: Study of the human microbiome extends beyond the digestive tract. Researchers, including those at MIT, are looking into the role the microbiome plays in things like super bugs and certain diseases. So expect lots of stories and much more gross science in the future.

That's it for this episode of the *Slice of MIT* podcast. But the story doesn't have to stop here. We want to hear your favorite stories of gross science. Tweet us your favorite stories on Twitter @MIT_alumni. That's MIT underscore alumni. Special thanks to Mark Smith and the team OpenBiome, as well as a special thanks to our squeamish listeners who made it to the end of the podcast.

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