The human microbiome is one of the most fascinating areas of science and medicine, and we’re just beginning to scratch the surface. Jack Gilbert is the Faculty Director at the Microbiome Center and a Professor at the University of Chicago; his research focuses mainly on microbial ecosystems, and in 2014, his thought experiment on a ‘World Without Microbes’ went viral in the microbiology community — Jack recently appeared in a video on the subject at https://youtu.be/80tPR5HH9Zo. In 2017, Jack co-authored the popular science book “Dirt is Good: The advantage of germs for your child’s developing immune system.”

Mark Smith is a leader in the field of Fecal Microbiota Transplantation, or FMT — one of the most buzzworthy practices in bacterial research. In 2012, Mark founded the nonprofit OpenBiome to expand the study and application of fecal transplants to patients suffering from diseases like infection from Clostridium difficile, or C. diff, which kills tens of thousands of people in the US each year. He now serves as the CEO of Finch Therapeutics Group, a mission-driven microbiome engineering company pursuing the first FDA approved FMT product. Mark featured in a video on the topic of FMTs available at https://youtu.be/ZZxRp-f3EjY.

As us anything about the microbiome and the study of gut bacteria!

Is there a known or suspected link between the condition of the gut microbiome and auto-immune conditions? I understand a large part of the immune system resides in the gut, and I wonder how the two systems interact. Is ther a relationship between the microbiome and human immune systems that can affect autoimmunity? Thank you for your AMA.

Learn2Web

There are a number of papers illustrating the association between the gut microbiome and various autoimmune/inflammatory diseases (for example this work in IBD). These efforts show that patients with certain inflammatory diseases have distinct microbiomes, but it is unclear whether the disease drives these changes or whether the microbiome does. One of the most exciting areas in the field right now is trying to move beyond these correlations to identify causal links. My colleagues and I are actively engaged in a number of clinical trials evaluating the impact of transferring microbes from healthy donors to patients suffering from inflammatory disease to try to identify whether changing the microbiome changes the disease. In ulcerative colitis, there is convincing data from randomized studies suggesting that this may work (e.g. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)30182-4/abstract). I’m very excited for what will learn on this topic in the years ahead! -Mark

Thank you for doing this AMA.
Usually after you have done a course of antibiotics there would be damage to the microbiome in our gut. My question is what is the best way to help it in recovering from the antibiotic drugs and if there is any way to reduce the damage done before or while a person is taking the antibiotics?

Naturedrag

I'm not aware of any safe approaches to accelerating the recovery of the microbiome following antibiotic exposure. OpenBiome has an ongoing study with the CDC in which patients in long-term care facilities at high risk for antibiotic exposure bank their stool on entry into the study and then get their own stool back (or a placebo) after antibiotics. This is the first step towards a process of autologous microbiome banking to accelerate recovery of the microbiome after antibiotics, but it's a long way off from becoming a practical reality. Until then, the best approach is to practice good antibiotic stewardship and ensure that antibiotics are really necessary before using them. -Mark

Thank you for doing this AMA.

Usually after you have done a course of antibiotics there would be damage to the microbiome in our gut. My question is what is the best way to help it in recovering from the antibiotic drugs and if there is any way to reduce the damage done before or while a person is taking the antibiotics?

Naturedrag

This is tricky to answer There is not enough evidence to determine the most appropriate way of recovering from antibiotics. However, in surgery we tend to try and get back to feeding the gut microbiome as quickly as possible. If we put out patients, who have been starved, given antibiotics, and cut open, food by mouth, as quickly as possible they tend to get better as quickly, and their microbiome returns to their 'healthy' state quicker. See here for more info: https://youtu.be/QRynQinhABw

Jack

I realize that the science on microbiome-targeted nutrition is far from settled, and that every person's microbiome is different. But as a best-guess universal suggestion, are there any foods that the general population should be eating for microbiome health? Onions, garlic, and leeks? Yogurt? Soluble fiber?

drsjsmith

Although the individualized nature of the link between diet and the microbiome is still emerging (e.g. https://www.ncbi.nlm.nih.gov/pubmed/26590418) there do appear to be some foods that may have general benefits across many microbiota conformations, with dietary fiber being chief among them. Dietary fiber is critical because it is a substrate for production of short chain fatty acids like butyrate which play an important role in promoting barrier function and regulating the immune response. -Mark

To you guys, what is the strangest link between the gut microbiome and maintaining human health? For instance, I was pretty impressed when I read that our gut microbiome drives the evolution of social behavior in humans.

blueoreosandmilk

I agree that the gut-brain axis is extremely interesting. I think one of the stranger links that I've seen is the anecdotal links between the microbiome and alopecia universalis (e.g. total baldness) first identified by colleen kelly (https://acgcasereports.qi.org/hair-growth-in-two-alopecia-patients-after-
All my friends drink apple cider vinegar "to maximize healthy bacteria" in their gut, is this a "one trick doctor's don't want you to know!" or are they stupid or is it something in between?

PM Me Your WorkFiles

I have seen this idea purported as well, but when I looked for ANY evidence that this was the case I could find nothing. I would argue that there is no specific reason why apple cider vinegar would have any substantial impact on the gut microbiome, the pH would not influence colonic bacteria, and the nutrients present are unlikely to have any specific pre-biotic effects over other foods. So I cannot even rationalize a mechanism of action as to why it worked.

However, remember 'belief' is a powerful thing, and the placebo effect is real.

Jack

Interesting. I've never heard of this practice before. I imagine the idea is to add an external source of acetate as a substrate for conversion into other short chain fatty acids. I would imagine that if consumed orally the acetate would be absorbed in the upper GI tract and never make it to its intended location. Along the way, the low pH could do significant damage to the epithelial layer of your mouth and esophagus, so while the idea has some conceptual logic to it, I think it is unlikely to have its intended impact and it may actually cause harm (though of course, I can't offer any medical advice!) - Mark

Can you speak to what links there are between gut biome and mental health? And also links to autism, which I read has been established?

Thank you for your time.

sutree1

Autism is a complex disease - I have an autistic son - and is a broad spectrum of conditions. Many autistic kids have significant GI problems, like constipation or diarrhea. Bacteria in the gut influence inflammation which can influence how the brain functions and develops. Also bacteria produce neurotransmitters in the gut, which are sensed by the nervous system, which sends messages to the brain and as such influences cognition. So thats also VERY complicated.

Yes there has been one clinical study which demonstrated in a population of 16 kids that fecal microbiome transplant could be effective in alleviating some of the gut symptoms and behavioral problems in kids with ASD, but that is VERY early work.

This article can help - https://www.sciencedirect.com/science/article/pii/S0092867413014864

Also look at this video: https://youtu.be/v12GBxN5kvQ and this one https://youtu.be/yhi6h_MmbC0
Thanks for doing this AMA!

I hear overuse of antibiotics is bad for the human microbiome. Can this damage be permanent?

Do we have any idea what makes a healthy microbiome, or how to optimize it for health dietarily or lifestyle-wise?

Why hasn’t there been more research on this in the past? Were there technological hurdles? Or did we simply not think the microbiome has a big influence?

Would you be able to take a guess on how much influence the microbiome has on human health?

Thanks!

logicallyzany

While we generally compare the microbiome between healthy and diseased people, there is still huge variability in the microbiome in healthy people, so that a 'healthy microbiome' is hard to pin down. We do know that an abundance of certain species can be detrimental and so when we see them, we can say that there 'may' be a problem. However, predicting disease state or health from the microbiome is still a very complex science. When you have a specific thing to predict, that is measurable, like blood glucose for example, then the microbiome can be tied to that. BUT remember, health is very hard to quantify - are you healthy? how do you know? are you more healthy than me? So I would say we do not know if antibiotics lead to an unhealthy microbiome per se, let alone whether they cause long term damage. Of course though, they do disrupt the ecosystem in the gut, and so if you take antibiotics and this occurs when you have a sudden change to a bad diet, or you have a pathogen in the gut which is not affected by the antibiotic, then you are likely to have negative outcomes, which could have long term consequences.

Jack

Thanks for doing this AMA!

I hear overuse of antibiotics is bad for the human microbiome. Can this damage be permanent?

Do we have any idea what makes a healthy microbiome, or how to optimize it for health dietarily or lifestyle-wise?

Why hasn’t there been more research on this in the past? Were there technological hurdles? Or did we simply not think the microbiome has a big influence?

Would you be able to take a guess on how much influence the microbiome has on human health?

Thanks!

logicallyzany

Great questions. On antibiotics, we don't know whether the impact is permanent, but there is significant epidemiological data that suggests that early childhood exposure to antibiotics has significant impacts (e.g. on obesity) later in life ([https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4836077/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4836077/)).

I don't think we have great actionable insights yet on what makes a healthy microbiome, though a balanced diet rich in fiber and avoiding exposure to antibiotics both seem important.

I believe that the gap in research was largely driven by technological hurdles as you suggest. With the advent of low cost high-throughput sequencing technologies, we've been able to interrogate the microbiome in ways that just weren't possible more than 10 years ago.
Once the gut bacteria changes, for instance, all of a sudden being sensitive to gluten, can it be changed back to normal.

millertyme007

There is absolutely no evidence that bacteria in the gut play any role in gluten sensitivity - although there are some small studies that have suggested that there is a correlation between microbial community structure and gluten sensitivity - but that doesn't mean that they have a causal role. Gluten sensitivity will cause an inflammatory reaction in the gut that could alter the microbiome.

Jack

Have you guys found out what bacterium causes those awful farts when you have been drinking?

MegaPompeo\n
actually some interesting data on this - sulfate reducers producing hydrogen sulfide. But it is not clear what causes them to ramp up production.

Jack

What is the current status of research into the effectiveness of fecal transplant? Is there some hope of the procedure being adopted on a wider scale?

newtonrox

There are only a few well controlled studies that demonstrate that FMT could be effective in treating certain disease types, so it is not a catch-all cure for sickness. For Cdiff infection it can be highly effective, as Mark can tell you. There are also some very early studies suggesting it could be effective in other diseases, even seemingly unrelated ones such as Autism, but a lot more work needs to be done before it could be distributed more effectively.

Jack

What is the current status of research into the effectiveness of fecal transplant? Is there some hope of the procedure being adopted on a wider scale?

newtonrox

There is substantial research (much of it enabled by the great work of my colleagues at OpenBiome and Finch) evaluating fecal transplantation in a range of microbiome-associated indications. The most mature research has been done for recurrent C. difficile infections, where fecal transplants have been used to treat over 30,000 patients. There is also compelling early work in ulcerative colitis. Beyond these indications there are many small studies, but few broad efforts. -Mark

How relevant is FMT for mental disorders?

potpourris
There are only a few human studies that suggest an effect - the one in autism I mentioned above (https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-016-0225-7), but not many others that are well controlled and are indicative of a specific effect. So it's hard. MOST of the work we have from this is in animals.

Jack

I know there is some research pointing to negative effects of c-sections on the microbiome of the infant. Is there any way to reverse this damage?

Also, if the mother herself was born of a c-section, is there any research on if there is a benefit to the baby at that point in a vaginal birth?

monkeydave

There is limit evidence that C-section has such a dramatic effect that any damage is irreversible with a healthy lifestyle. However, there is a clinical trial ongoing at NYU to determine is vaginal seeding is effective in preventing the onset of diseases that are elevated in c-section babies - see this article for an idea of the controversy - https://www.the-scientist.com/?articles.view/articleNo/45505/title/Opinion--A-Mother-s-Microbes/

Right now though I would suggest that a healthy lifestyle and diet will ensure that any negative consequences of c-section delivery should be countered.

Jack

How hard is it to actually detect and measure a person's micro biom of the intestines? I have heard that a lot of the bacteria die off rather quickly when exposed to air and that would be the reason a stool sample is not the best way to determine a person's micro biom. Is there truth to that?

Thank you.

SgtDirge

Yes when you poop some of the bacteria die, but their molecular signatures (the bacterial DNA) remains long enough that we can still detect them. Also there are ways to keep the bacteria inside the poop alive. There is a company called The BioCollective, which I cofounded (so a Conflict of Interest maybe), but they designed a poop collection kit for at home collection that is designed to ensure the bugs stay alive.

Jack

How hard is it to actually detect and measure a person's micro biom of the intestines? I have heard that a lot of the bacteria die off rather quickly when exposed to air and that would be the reason a stool sample is not the best way to determine a person's micro biom. Is there truth to that?

Thank you.

SgtDirge

It's true that it is difficult to characterize the microbiome. Much of the work to date has relied on high-throughput DNA sequencing to solve the challenges associated with growing these bacteria that you alluded to above. -Mark
Do you believe we'll go beyond 'scratching the surface' and understand causal relationships between the microbiome and human health without being able to accurately model microbial interactions (e.g. cross-feeding interactions between bifidobacteria and butyrate-producing colon bacteria) and their effects on various biomarkers?

verveandfervor

I sincerely hope we are already doing that. While the bulk of research is still correlative and discovery based, many studies are exploring the causal mechanisms and making actionable findings. In fact we have a review coming out in Nature Medicine soon which highlights a lot of these points - moving beyond correlation.

jack

I heard about FMTs going through college a few years ago! It's such an interesting approach to understanding the digestive system.

What's a realistic timeline for FMTs to be an approved practice to restore healthy gut activity?

What are some of the most difficult hurdles you are encountering towards this end?

ashpens

Getting FDA approval will probably take 3-4 years, with the most difficult hurdles being conducting large, well-controlled trials to demonstrate safety and efficacy to the FDA. -Mark

Thank you for this AMA.

Where do you see research on this topic headed in the next 5 to 10 years?

BoxingHare

Read this https://www.nature.com/articles/nature25019

Jack

What is the most important bacteria in the entire stomach? Also I hope you are having a wonderful day!

Maxz963

No such thing - no single organism is most important - more important is the community and their overall relationship to the host.

jack

Drinking wine has been proven to reduce risk of heart disease. Is this because of interaction between the gut biome and wine?

teemalph

not clear yet - there is some research in this area, but the results are inconclusive.
But drinks wine - its nice!

Jack

I am scared of eating Danone products that got their super stable and powerful bifidobacterium there, some exclusive one. I don't want it to outperform others in my gut. Can it?

s_____aaaa

no. not at all.

jack