

Perspectives On The Microbiome Industry

As we continue with our blog series we had the delight of interviewing Chris Damman from the Bill & Melinda Gates Foundation and discussed his career, research, his vision of the future, and how it all started.



Christopher Damman
Senior Program Officer,
Global Health
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Foundation**

Chris earned his M.D. from Columbia University and is board certified in both Internal Medicine and Gastroenterology. He wears hats as a senior program officer for the Bill & Melinda Gates Foundation and a clinical assistant professor of gastroenterology and medicine at University of Washington. When asked how it all started for him, he jokes that his family may have suspected from the earliest of ages by his sense of humor that gastroenterology was a natural fit.

Although this may be true, it sounds like what may have launched him in earnest on his path was a lecture for an infectious disease course during medical school and a suggestion by his professor to read the book *Plague Time - The New Germ Theory of Disease*, written by Paul Ewald. "At the time, there was a lot of focus on human genetics and we were in the midst of the human genome project. Dr. Ewald put forward a really compelling argument from an evolutionary standpoint, which made great sense to me. There was more going on in the background of these diseases and he pointed his finger at microbes. That was kind of the prelude to the microbiome back in 2002," Chris explained.

When it came time to choose a subspecialty, after pursuing adult medicine out of medical school, he was faced with a decision between

studying infectious disease, which had always intrigued him, and gastroenterology. As he presents it, "It was a choice between hunting for pathogens in the jungles of the developing world or pursuing the commensal microbes in the jungles of the gut. I choose the jungles of the gut at the time, but fate works in a funny way - and here I am back traveling the world and helping folks in places where help is really needed. It is incredibly gratifying!"

Understanding the microbiome was a passion for Chris going back to medical school and has percolated throughout his residency and fellowship, ultimately culminating in the research he began doing at UW. His lens on the issue has evolved over time, and he is now taking all of those perspectives and applying them to the developing world through his work with the Gates Foundation. As he moves from one 3 letter acronym to another - Inflammatory Bowel Disease (IBD) to Environmental Enteric Dysfunction (EED) - the letters are different but many of the underlying principles are very similar.

At the University of Washington, his work spans both the clinical and the research worlds. He began working in translational endeavors with a series of small pilot trials on understanding how diet and the microbiome may be involved in inflammatory bowel disease.

One of the first pilots was back during the very early fecal transplant era, looking at ulcerative colitis. The primary aim was to find if stool from another donor could engraft with ulcerative colitis. The second major study, which is still ongoing, is looking at dietary interventions in IBD. "Gut issues can be treated with microbes or you can treat them with nutrition - the two intersect in really fascinating and important ways," says Chris.

"I like to think I have one big toe in the clinical arena still and UW is incredibly supportive in continuing clinical work there. Being in the trenches inspires me in real ways. Next-generation therapies being developed for IBD may apply to EED. There may be common threads with the underlying disease processes of the two."

When asked what an average day in the life is like he modestly describes it as "busy." His days revolve around people's schedules from all over the world that don't always line up. Often rising at 5:30 A.M. to start calls by 6, he pauses his mornings for family breakfast and a parental tag-team to get his three girls off to school. After a run or bus ride into work, his days consist of meetings, phone conversations and, on some days, seeing patients - and those are days when he is in the office or clinic. He estimates that 25% of his days consist of traveling to conferences, such as the one he recently spoke at with the Microbiome Movement, and

visiting parts of the world running clinical trials where he works with the Gates Foundation's grantees to develop next-generation interventions.

Chris explains that there is immense value in visiting clinical study sites. He notes how interventions that may work great here in the United States can be completely impractical for the developing world, such as giving an expensive and difficult-to-dose therapy to a child whose mother is worrying about just feeding her children. "It can be complicated by the conditions that the people are living in. While health is a priority, there are basic needs that need to be met. Seeing all those realities really help refine my perspectives and approaches."

"They say 'A week in the lab can save you a day in the library'... I might say a year of trying to develop a new therapy might save you a week of visiting the developing world and seeing how things are. It really is the invaluable nature of going and seeing it firsthand."

One of the studies he is very excited about is the MORDOR study in Malawi, Niger, and Tanzania, where researchers are examining the use of oral azithromycin to reduce mortality rates in young children. Chris explains that there are results showing all-cause mortality improvements with just a single dose given every 6 months across the communities. This is a massive response observed for such an intervention. One

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of the ongoing efforts is to understand how azithromycin is working to achieve such a big impact in the first place. Chris thinks that in addition to the drug's antimicrobial and microbiome-modulating properties, there may be some other indirect benefits that explain the positive impact on mortality rates. Looking at other fields for possible explanations, there have been some benefits with the use of azithromycin for patients with cystic fibrosis and research showing that it alters mucosal health through direct modulation of the immune system and the cells that produce mucus.

Among Gates Foundation-funded work, he references Dr. Don Ingber's group at the Wyss Institute at Harvard University that is doing modeling work to remove the complexity of the microbiome and pathogens by using the gut-on-a-chip model to see what the drug is doing in isolation to the gut itself. The findings are intriguing as they show how the drug may alter the barrier function within the lining of the gut by increasing mucus and antimicrobial peptide production.

Chris believes that all of this research is significant for developing next-generation interventions. He explains, "It is pretty amazing when you think about it, that giving a single dose of azithromycin – just a single dose – can have such a profound and lasting effect. These kids are in environments lacking sanitation with pathogens everywhere. While one might imagine a 'pathogen holiday,' it is not going to get rid of pathogens forever. There may be additional effects where you may be augmenting the gut barrier that helps prevent the pathogens from coming back right away."

His excitement for the current research continues as he expands on the co-op of 3 institutions & hospitals – International Centre for Diarrhoeal Disease Research in Bangladesh (icddr,b) led by Dr. Tahmeed Ahmed, Aga Khan

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University in Pakistan led by Dr. Asad Ali, and Lusaka University in Zambia led by Dr. Paul Kelly – where they are trying to see what is happening in the gut of kids with malnutrition and stunting. This is something that researchers haven't been able to do before. The question for Chris is, how can we treat something when we don't really know what it is? "The very name of Environmental Enteric Dysfunction (EED) connotes ambiguity and lack of definition. Dysfunction? What does dysfunction precisely mean?" In these 3 sites, where kids don't respond to nutritional therapy, they are actually collecting aspirates and sequencing the microbiome, conducting biopsies, and looking at the gut tissue to examine what may be wrong with it, why it is inflamed and why it has decreased absorption capacity. His hope is that the important lessons coming out of the research will lead not just to treating pathogens, which is what has been done historically, but treating the underlying biological vulnerability which in part stems from the gut and microbiome. The hope is that this will lead to the knowledge of what levers to move, whether it be re-equilibrating the microbiome or reestablishing the barrier function in a long-term and sustainable manner.

Beyond the conventional endoscopy deployed above, pilot studies led by Dr. Asad Ali at Aga Khan University are beginning to implement a new tethered capsule technology that does not require kids to be traditionally sedated, as it can be passed through the nose. Chris believes

that this technology, which is being masterminded by Dr. Gary Tearney at the Ragon Institute of Massachusetts General Hospital, "will rocket our understanding of EED and malnutrition and the underlying vulnerabilities that predispose children to these kinds of infections in the first place. It transforms our approach from one that is reactionary – to the pneumonias and diarrheas – into one that is a little more preventative and proactive." The ability to conduct tests without being so invasive will allow them to test more kids both before and after the intervention and can even be used on non-sick kids to compile a better set of control data.

When asked about how the above technologies will lead to new therapies in nutrition and the microbiome, Chris responds, "Sampling the small intestine will help us understand how food intersects with the microbiome and gut in parts of the intestine that historically have been inaccessible to researchers. It will teach us how we can use food and other therapeutic approaches to grow a happy healthy microbiome in the small intestine where nutrient absorption occurs and a healthy barrier protect us from pathogenic organisms."

One place the tethered capsule might be applied in the future is in already ongoing Gates Foundation-sponsored work at Washington University in St. Louis and the International Centre for Diarrhoeal Disease Research in Bangladesh led by Dr. Jeff Gordon and Dr. Tahmeed Ahmed.

This collaboration, at the intersection of diet and microbiome, is piloting a new microbiome-targeted ready-to-use therapeutic food based on locally sourced ingredients for rehabilitating children with acute malnutrition.

In addition to dietary interventions, Chris explains, “There may also be microbial holes that exist in the microbiome due to the Westernization of diet and other factors like indiscriminate use of antibiotics. How do we get those critical bugs back to individuals that may already be missing? This will be a major theme moving forward.” Indeed, Chris speaks of the “pandas” of the microbiome that one might consider endangered species in the gut, and the work the Gates Foundation is conducting with pioneering companies like Evolve BioSystems, Vedanta Biosciences, and OpenBiome that are piloting next-generation therapies for replacing some of these species.

According to Chris, one of the big challenges in the developing world, and even in the United States, is that there are populations that do not have access to or cannot afford a varied diet of whole nutritional foods, so many of them can only obtain more affordable, often processed options with longer shelf lives. These foods in their current forms are frequently missing important dietary components including certain micronutrients, polyphenols, and fibers, and many contain components that improve shelf

life but are potentially harmful to gut-health. There is also a need for research looking at not just the amount of protein, carbohydrates, and fats in foods but the right types of proteins, carbohydrates, and fats.

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Chris believes that whole foods are always preferred but that next-generation processed foods will be an important part of the solution in delivering affordable nutrition to difficult-to-reach parts of the world. He speaks about “Food 3.0,” where the next-generation of processed foods will be mindful of these components in a microbiome and gut-friendly way. This could be an area where organizations like the Gates Foundation and the Center for Microbiome Innovation can work with a few big food companies who are willing to lead the charge to establish a workable approach.

When it comes to personal nutrition, Chris acknowledges there is sometimes a disconnect between what you know you should do and what you actually do. He recommends that his patients stick to a few simple parameters when shopping: purchase from the store’s perimeter where the whole foods are, park as far away from the entrance as you can get, and always use the stairs when possible. He also appreciates and tries to follow the advice of Michael Pollan in the book *The Omnivore’s Dilemma*: “Eat food, not too much, mostly plants.” As recent research suggests, Chris places an equal emphasis on recognizing the importance of exercise, sleep, and maintaining low stress levels for a healthy microbiome. He is struck by how fortunate he is – on a good day, he is able to follow his own advice and buy lots of whole foods from the grocery store. He is also struck by how privileged he is to be part the Gates team and this world-class network of investigators – playing a small part to help move this foundational work forward.

We, in turn, are struck by how privileged we are to have such a great microbiome science advocate in Chris!

Visit our [Microbiome Movement media hub](#) for the latest perspectives on the microbiome from industry, academia and the clinic.