00:00:04:14 - 00:00:13:10

Clare

Hello and welcome. I'm Clare and you're listening to Microbe Talk, the podcast by the microbiology society.

00:00:13:12 - 00:00:43:04

Clare

Everyday actions, such as eating, toothbrushing or applying cosmetics inherently modulate our microbiome. Advances in sequencing technologies also now facilitate detailed microbial profiling, which drives international microbiome targeted product development. This inspired Aline Metris and Lindsay Hall to host an academic industry workshop held here at the Microbiology Society offices in January 2024, and published their review inspired by discussions from the workshop.

00:00:43:06 - 00:01:09:20

Clare

Their paper, Assessing the Safety of Microbiome Perturbations, published in Microbial Genomics, explores oral skin and gut microbiomes, addressing the challenges of evaluating microbiome perturbations, focusing on the potential long-term implications. So, for this episode of Microbe Talk we invited them both back to the Microbiology Society offices to talk to us about their publication.

00:01:09:22 - 00:01:25:24

Clare

Hi, Aline. Lindsay, it's lovely to have you both in the offices today. And a good place to start is an introduction. So could you both please introduce yourselves, your institutions? And tell us about your research interests? Lindsay, would you like to start?

00:01:26:01 - 00:01:49:18

Lindsay

Yeah. Hey, everybody. I'm really pleased to be back down at the microbiology offices. And so I'm Professor Lindsay Hall, I'm chair of microbiome research at the University of Birmingham. And I'm also a group leader at the Quorum Institute in Norwich in the UK. And research interests very much revolve around the microbiome and specifically looking at the early life developmental window and looking at maternal and infant health.

00:01:49:20 - 00:01:54:04

Clare

Aline, it's lovely to have you in the office as well today. Could you please introduce yourself?

00:01:54:09 - 00:02:20:20

Aline

Hello. Thank you for to invite me as well. So my name is Aline Metris. I work at the safety and regulatory science at Unilever. So, Unilever is a FMcG, so it's a company producing goods like cosmetics, home care products and food. I have been working there for seven years and since joining I've been working more on looking at the safety of the microbiome.

00:02:20:22 - 00:02:30:06

Aline

Generally, my, research interest is around, modelling microbes. And so I work in a food safety triangle for preservation.

00:02:30:06 - 00:02:46:16

Clare

Amazing. And thank you again for coming in. So you're, of course, here to speak about your recent publication. But before we go into the paper, could you please start with explaining what the microbiome is? And what microbiome perturbations are? Lindsay, can we start with you?

00:02:46:18 - 00:03:14:21

Lindsay

Yeah. Perfect. So I guess we'll talk about microbiomes. And specifically for this, it's human associated microbiomes. So when we see a microbiome, what we normally mean is a microbial community, community of microorganisms. And that's because the body is home to incredible communities of Michael organisms microbiomes both on and within the body. So the skin and the gut and also the oral cavity as well, plus other body sites and these microbial communities are very complex.

00:03:14:21 - 00:03:34:06

Lindsay

There's trillions and trillions of different types of microbes, but they're fundamentally important for host health, both short term and longer term. As well. And they can do this by modulating the immune system, helping digest the food that we eat. And they're even important for cognitive development as well, which is why we're very interested in microbiomes in general.

00:03:34:08 - 00:03:40:24

Clare

And only in the you able to, provide some insight onto what microbiome perturbations.

00:03:41:01 - 00:04:02:15

Aline

So actually, without realizing it, we are always better with the microbiome, even just eating you, changing your gut microbiome. But also when you apply cosmetics products, for instance, on your skin, deodorant typically really modify your microbiome. Also, when you brush your teeth, for instance, you are changing the oral plaque you have on your teeth.

00:04:02:17 - 00:04:14:09

Clare

Interesting. So why do you think it's popular? I think to talk about the microbiome right now. I think it's something that comes up quite a bit in the news. Why do you think it's come to the forefront of the conversation?

00:04:14:11 - 00:04:37:00

Lindsay

Well, I think the microbiome is really at the forefront because, I mean, as I explained, the potentially program or help us do lots of different bodily functions, and because they're so important, that's why I think there's such big interest in this sphere, including obviously, product development, which we'll get on to, but just more generally about how these microbes do their jobs and why they're really fundamentally important for health.

00:04:37:02 - 00:04:48:16

Lindsay

But as already discussed, also perturbations. So that may also be associated with them, disease outcomes as well. And that's kind of why there's just this more broader general interest in the topic.

00:04:48:18 - 00:05:03:18

Clare

And it is of course very interesting as well. So the process which led to the paper began with an academic industry workshop held at the Microbiology Society, which you both hosted. Eileen, could you explain what motivated you to host the workshop?

00:05:03:20 - 00:05:36:04

Aline

We were looking into a platform where we could talk about the scientific challenge, linked to the microbiome. So it's actually quite a recent science, if you think about it. The Human Microbiome Project is only a bit more than ten years old. And, this is really new science on raise lots of technical challenges associated to it. And we're really looking for a, a platform where we could talk between the scientists, industry, etc. to, try to, see where the science is really.

00:05:36:10 - 00:05:51:00

Clare

And the workshop was attended by participants from academia, industry and regulatory bodies with expertise ranging from microbiology to artificial intelligence. Why do you think then it's important for all of these different groups to collaborate on this issue?

00:05:51:03 - 00:06:14:19

Aline

So this thing, it's very multidisciplinary. So because we are looking at, sequencing data to measure the microbiome, we need to understand very hot. So we need biology. We need people who can interpret the data. So I think we need to really meet the disciplinary approach. But also we need to have the, perspective of all kind of participants from the consumer and the scientist.

00:06:14:24 - 00:06:48:07

Lindsay

We also need multidisciplinary expertise in there. And I think what was very important here, that was a joint academic industry workshop. So everyone's coming in with different expertise, but there's different perspectives because people work in different settings. So I think not just in terms of thinking about the disciplines specific interdisciplinary nature of the of the workshop, but actually having getting academics and industry in the same room together, I think was incredibly important given the topic about thinking about how we assess safety of new microbiome targeting products.

00:06:48:09 - 00:06:53:14

Clare

What would you say was the role of the microbiology society in curating the workshop?

00:06:53:16 - 00:07:07:21

Aline

I think you you were a really great in, putting together. So, academics and industry, acting as a neutral platform to, to talk to people. And also, the organization was a top notch.

00:07:07:23 - 00:07:27:12

Lindsay

Yeah. No. And I think, again, it's the reach of the microbiology society as well. And obviously, part of the workshop was actually soliciting for people to kind of see, I would be interested in attending. So that's maybe also one of the reasons why we had such great engagement at the workshop was because there was members already aware that this was coming up, and then they could put an expression of interest to see that they were interested in joining.

00:07:27:18 - 00:07:45:00

Lindsay

And that's the joy, the fact that the microbiology society, there's like so many members and they all have slightly different topics or focuses. So that was brilliant to kind of bring everybody in as well. And as you say, kind of that neutral platform that can kind of bring people together. I'm under an umbrella as part of the workshop and then just kind of facilitate that going forward.

00:07:45:00 - 00:07:46:16

Lindsay

Yeah. Was was excellent.

00:07:46:18 - 00:07:53:04

Clare

What was it like being in that room, collaborating in person just from your experience? What did it feel like?

00:07:53:05 - 00:08:02:07

Aline

It's really good. And actually I was surprised how engaged everybody was on it. It was quite incredible, actually. Incredible experience. Very intense.

00:08:02:09 - 00:08:22:24

Lindsay

Yeah, absolutely. Very intense. But I would agree, I think the engagement was really outstanding. I've been part of many other workshops, and you don't normally get that level of excitement and enthusiasm and people really actually wanting to work through some of the key topics that we proposed. So and it was just really nice to hear from leading experts as well.

00:08:22:24 - 00:08:29:06

Lindsay

And then just having a really open, frank conversation between all participants over the course of the workshop.

00:08:29:06 - 00:08:38:11

Aline

And even we was nice to hear. One of the professor told me, oh, this is a longer. I never thought about it this way. So for me, that was the best compliment I could have.

00:08:38:15 - 00:08:52:02

Clare

I say, wonderful to hear and you know, your experiences and positivity coming from the workshop isn't the only thing that came out of the workshop. Of course, your paper did well go into, I suppose, the details of it. But could you give us a brief overview of the paper?

00:08:52:04 - 00:09:14:11

Aline

Yeah. So the paper, take over what drew discussion were workshop. So in the first part, we the presentation about the overall skin and gut microbiome by experts. Then we talked about, clinical studies. Where we can help us to understand more about the microbiome. We talked about AI and also in vitro models.

00:09:14:13 - 00:09:18:13

Clare

And so why do you think it's important to publish the findings in the background of the workshop?

00:09:18:17 - 00:09:31:09

Aline

Well, it's important to get the word out that there's a, community of people thinking about this question, and we look forward to get more people involved. So it's the best way to reach out.

00:09:31:11 - 00:09:56:00

Lindsay

Yeah. And I think, I mean, the workshop and we chat about the dedication, enthusiasm of the participants, it's really nice to actually have something written down and published as a record of what we've done and really actually thinking longer term, for example, it's really important to have that out there and open access so people can read it, get involved and think about how they might want to like, move forward in the kind of safety assessment microbiome space.

00:09:56:02 - 00:10:17:06

Clare

Yeah, it'd be great. This could be used as sort of a useful resource for people that couldn't attend. And yeah, that's, that's very good point. So microbiomes can be influenced and changed by lots of different things, such as new diet cosmetics, as you, as you mentioned earlier. So why do you think it's important to assess the safety of microbiome perturbations?

00:10:17:12 - 00:10:41:00

Lindsay

So assessing safety when we're changing our microbes every day just by the things that we do, I think it's really important because these microbes are fundamentally important for our overall health and well-being. Yes. In terms of, for example, like you can take a course of antibiotic, I mean, one of the and hopefully that's going to get rid of the nasty back to your pathogen that you have.

00:10:41:02 - 00:11:10:12

Lindsay

But one of the consequences of taking antibiotics is they potentially also or specifically target beneficial members of microbiomes. And of course, if we lose these beneficial bacteria, then there might be consequences for the microbial ecosystem itself, but also in terms of thinking about what that might mean for the host as well. So for example, taking a course of antibiotics,

particularly in early life, has been linked to higher incidences of inflammatory conditions like Crohn's disease and colitis later on.

00:11:10:14 - 00:11:35:14

Lindsay

So we already know that, for example, and biotics do that. And but obviously they're fundamentally really important to take medical Marvel. But we need to take them in the right way. But with no and I guess the increasing interest in microbiomes and targeting them from a therapeutic or health perspective, it's really important that we put a clear safety framework around what might they do.

00:11:35:16 - 00:11:46:19

Lindsay

So yes, we want them to have maybe a particular positive impact, but we also need to make sure that there's not any off target effects, for example. And that's why assessing safety is really, really important.

00:11:46:21 - 00:11:56:09

Clare

Absolutely. So how have clinical studies help researchers to understand the association of the microbiome to, to health and disease.

00:11:56:11 - 00:12:20:00

Lindsay

So, unsurprisingly, clinical studies are really important because we're talking about human microbiomes. And so it's pretty good to have a look at humans. But of course we are limited with what we can do as part of clinical studies. But there's been numerous different studies that have shown that microbiomes, if they're perturbed or changed in a particular disease setting, they might be then associated with specific clinical outcomes.

00:12:20:06 - 00:12:38:19

Lindsay

But for the vast majority of these, this is just an association. It's not causation. And that's I guess, one of the limitations of just using human and human subjects is that we can't necessarily, you know, is a chicken or the egg. It's quite hard to disentangle that from a participation perspective. So those clinical studies have been fundamentally important.

00:12:38:19 - 00:12:56:06

Lindsay

And understanding that microbiomes are important. And if we change them there's consequences. But actually what those consequences are or how potentially long term the are those consequences. That's potentially where we need other methods models to come in to help those I guess more nitty gritty questions.

00:12:56:06 - 00:13:03:15

Clare

And just on that point, I mean, what is the kind of current situation with clinical studies assessing, the safety of microbiome perturbations?

00:13:03:15 - 00:13:23:10

Lindsay

So at the moment, I guess there's not really any clinical studies are actually answering that question specifically. And of course, clinical study and design can be different depending on what the question you you have, what your patient cohort is, for example. And they're normally very expensive. They're very long term. So actually spending time at the beginning to really carefully design them is really important.

00:13:23:10 - 00:13:45:20

Lindsay

In fact, that's one of the topics we discuss or put forward in the review as well. And I think the other thing that's important is is assessing not just short term perturbations but longer term ones as well. So thinking a little bit innovatively about how we can maybe do longer term clinical studies without them costing a huge amount of money, and making sure that we capture additional information.

00:13:45:20 - 00:13:50:02

Lindsay

Again, that's some of the kind of specifics that we talk about in the review.

00:13:50:04 - 00:13:56:06

Clare

So how can clinical studies, along with AI help us to understand the safety of intervention?

00:13:56:06 - 00:14:22:15

Aline

And then one of the challenges at the moment is we don't really have biomarkers of health from disease. So nothing to say. This is really what matters for health or for disease. So we discussed that if we use, human studies, what we call longitudinal, that means that we measure with time what's happening to the microbiome. And we use technology like AI to put together all kinds of data, looking also at the host.

00:14:22:17 - 00:14:47:16

Aline

So like me, to meet up or to mix medications. We don't mix metagenomics all of a meta omics possible. Looking at this data is very tricky because we are very different. But if you use new technology like AI, we might be there an opportunity to look at really what is a function of a microbiome for health in relation to the host is important or detrimental.

00:14:47:22 - 00:15:07:21

Aline

So this is something we discuss in a paper how we could leverage today's new technology. All of this comes with an investment in being transparent about the data, recording the head of state of the patient, and also the data in database that can be retrieved. So big analysis.

00:15:07:23 - 00:15:16:23

Clare

Amazing. And so in vitro models. What's the potential and the limitations of using in vitro models to study the microbiome.

00:15:17:00 - 00:15:42:02

Lindsay

So I think one of the things that's really important, particularly from our product development perspective, is understanding how they work. And how they potentially influence the microbiome, and also how the influenced the host as well. And in vitro models provide a really strong platform to be able to understand those mechanistic differences, because they potentially scale. And I think we talked about the complexity of the microbiomes.

00:15:42:02 - 00:16:17:20

Lindsay

In vitro models are one way to be able to actually screen maybe multiple different types of products to understand what that might do in terms of from a microbiome perspective, but most importantly, how they might specifically target C are very specific immune pathway in the host. So they provide that level of rigor to understand what the consequences of those changes or if that microbiome targeting therapy, for example, in terms of limitations, I mean, all models, clinical studies, eye microbiome profiling, everything comes with its own limitations or biases as well.

00:16:17:22 - 00:16:45:24

Lindsay

And I think from our individual perspective, I think how we defined end points, as in what's potentially socially with health or what's associated with disease are detrimental. I think that's a challenge in the field at the moment. So I think the models are fantastic, but I think that's why, again, we need people to be working together, having an open dialog about how they can really be rigorously used in the context of assessing safety for microbiome targeting products.

00:16:46:01 - 00:17:02:02

Clare

Exactly. And I suppose that having events such as the ones that you hosted is a perfect platform opportunity to be able to discuss those kind of things and make sure that the understanding of each element of clinical studies is fully understood and used in the right way.

00:17:02:04 - 00:17:19:11

Lindsay

Exactly. And I think the advantage of the workshop as well, being in person and obviously having that open dialog, was the fact that people were able to also highlight and showcase cutting edge work that's happening at the moment as well. And that obviously gave food for thought for people that might not be working that area or working with those models.

00:17:19:11 - 00:17:41:16

Lindsay

They might be like, oh, I didn't know that that was available. And obviously that's also a really wonderful way to enhance networks and new collaborations going forward as well. So not just in terms of we all sit in a room and chat about it, but actually having those conversations will lead to and has led to specific new collaborations between either academic groups or academic industry or industry industry industry groups as well.

00:17:41:18 - 00:18:02:16

Clare

So in your paper, you suggest that continued scientific collaboration and public engagement are critical for long term microbiome monitoring, which is essential to advancing safety assessments of microbiome perturbations. What would you say is the current understanding of the microbiome from people outside of this very specific sphere?

00:18:02:18 - 00:18:22:09

Lindsay

So I think, I mean, we talked kind of at the beginning. I mean, the microbiome is a pretty hot topic that is in very much in the public eye. And that's why I think it's important to understand what the perceptions of the public are. So and of course, that's different depending on who you speak to because I mean, that's just that's just the nature of the game.

00:18:22:11 - 00:18:51:11

Lindsay

But I think by and large, I think there's a pretty good understanding by the general public about microbiomes. And they might be important. They may not necessarily understand the nuance, for example, why it's really important for us to be thinking about safety assessments, for example. But I think in general, I think it's it's pretty much out there and there's like, you know, articles, you know, different, topics are discussed kind of all the time, including on like TV for documentaries.

00:18:51:13 - 00:18:53:05

Lindsay

So I think it is very well understood.

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Clare

What would you say needs to be done in terms of public engagement?

00:18:57:10 - 00:19:13:15

Lindsay

I think for public engagement, I think it's really important just to kind of, I guess, give the basics about the microbiome and why they're important, because I think actually that gives a little bit of empowerment to the public as well, that they can actually take charge of their own microbiomes and actually think about what other things might be doing from an everyday perturbation perspective.

00:19:13:17 - 00:19:32:19

Lindsay

So I think that's just kind of a general, perspective. But I think for the work that we were doing, one thing that came out of the workshop for this was the fact that if we're monitoring long term safety, one of the way we can potentially do that is actually for the public or patients to be reporting findings or data back.

00:19:32:19 - 00:19:52:24

Lindsay

And the best way for us to do that and to actually get really high quality, I guess qualitative data as well as quantitative data is to make sure there there are kind of gauged and educated, understand more generally about the microbiome, and then they can share that amongst others peers that they know as well. And I think that's one way to actually have a wider engagement around the topic as well.

00:19:53:01 - 00:20:01:06

Clare

So they can be a tool as well. Yeah. And where do you both see the future of this work heading?

00:20:01:08 - 00:20:27:20

Aline

I think we've started to, put together a little community working on this topic, and I really hope we can carry on spreading the word. So growing the community, but also progressing with the, research, subject we already define that needs to go forward, like defining more in vitro model endpoint and having more data, meta data so that we can apply.

00:20:27:22 - 00:20:40:19

Aline

So it really it was really a pleasure to work with Lindsay. And, I hope we can carry on working, as an academic industry partner. Freedom from that.

00:20:40:21 - 00:20:59:06

Lindsay

Yeah. From my perspective, I think where we're going to go, I think this was we've not given any concrete guidance or guidelines in this review. That was not the point of the workshop that's going to take a little bit more work to be able to do. But it's the start of the conversation. And I think so we've got exactly some really key things that we probably want to move forward.

00:20:59:06 - 00:21:15:18

Lindsay

Maybe that might be targeted workshops, might be doing some webinars, a little bit of watch this space. But I think this is a really nice blueprint for kind of where we want to go. And I think more longer term, even thinking about from a regulatory perspective as well, engaging with policy. And this is just important to make sure that we capture that as well.

00:21:15:24 - 00:21:41:19

Lindsay

So I think it was great fun, a lot of work. But I think hopefully it's now going to move things forward. I think we talked about human microbiomes, for example, and there's some very specific topics that you think about that. But one of the other things that might come out about this is like people working in different microbiomes, for example, animal microbiomes might be also then thinking about, well, how do we think about safety assessment and that particular setting as well.

00:21:41:19 - 00:21:49:03

Lindsay

So it's also just sparking some ideas and just having setting off conversations as well. And we'll just see where we're at leads us.

00:21:49:05 - 00:22:06:13

Clare

And of course, if you're a member listening and you're interested in getting involved in this, in this type of work, you can of course publish with us. You can engage with some of the microbiology, society work that we're doing. Watch this space. Essentially. I think there's things coming up in the future that that you'd be interested in.

00:22:06:15 - 00:22:11:02

Clare

Thank you so much, Lindsay and Aline, for joining me today. It's been so lovely to have you.

00:22:11:04 - 00:22:12:15

Aline

Thank you for inviting us.

00:22:12:17 - 00:22:13:24

Lindsay

Thanks for having us.

00:22:14:01 - 00:22:30:15

Clare

Thank you so much to Lindsay and Aline for joining me on Microbe Talk today. If you'd like to read their paper, you can find it published in Microbial Genomics, or you can follow the link in the description.

You've been listening to Microbe Talk. If you like this episode, please leave a like or a comment wherever you're listening.