

Question & Answers during Webinar:

**Prof. Dragsted:**

Q: Regarding the data on alcohol, there have been reports that some individuals have microbiomes that can convert normal fruits into alcohol in the gut in the process of normal digestion. Is it possible that this may explain some of the discrepancy between reported and measured alcohol consumption?

A: I think so. However, the level is not known. I mean most cases are auto-brewery syndrome where people actually go around drunk all the time because of high alcohol production in the gut. Whether a low level of this production is common has not been investigated though we do have data and could go into that. I think that is an area we need to go into because the alcohol biomarkers differ much from all the other biomarkers in terms of how well they are in concordance with the dietary records.

Q: How would you address habitual (rather than recent) diet, as well as its interaction with microbiota and health outcomes?

A: Dirk Haller showed that the time course of food reaching the microbiome can differ quite a bit. It will take 4-6 hours before it reaches the large intestine. When I see a compound coming up around 4-6 hours after a meal I suspect it is a microbial product of some food component and an indication that the microbiota may be involved. If you have longer term exposures, for example eating the food regularly, then you will feed the microbiota on a regular basis. Firstly, the microbiota will then be used to this kind of food and will evolve additional functionality; the microbiota will improve in degrading your food and turning it into certain compounds reflecting this particular functionality. Secondly, you will also see biomarkers that take longer time to form. For instance, some of the ellagic acid degradation products are not seen until 48-72 h after the intake. So, for the urolithins, it will take some days until you see them excreted in the urine.

For all these compounds, the kinetics is really important for how we use them as biomarkers.

Q: Given that there are reports that microbiome shapes drug response, do you see potential in finding out which nutritional compounds might shape the gut microbiota in a way that benefits a favorable outcome? Obviously, as Prof. Haller has pointed out, we are still quite far from actually giving such support.

A: Yes and No. I completely agree with Dirk Haller on this point but we also have seen that when we study something like a Mediterranean diet study, we do see also some change in microbial metabolism towards a range of compounds that are expected to have beneficial health effects. The general advice on healthy diets seems to be correct in terms of also feeding your microbiota the right stuff. But if you want to go to the personal level, we are not there yet.

Q: How could the question of associating metabolite to pathway, and whether is from the host cells or from the microbiome?

A: That is a very difficult question. I mean you can always do in vitro incubation with the stool samples to see whether you can produce the compound. Even there, sometimes some of the microbiota does not survive being exposed to oxygen but the enzymes are still likely to exist. This is

one way to separate the microbial metabolites from the host's. We often try to figure out about this. We published a paper several years ago showing that when you have a cyclohexane ring it will gradually be metabolized into an aromatic ring. And whether this takes place with the microbiota enzymes or hepatic enzymes is still not clarified in the literature. So we come across biotransformation pathways that are unresolved in terms of whether the host and the microbiota has the required genes and enzymes.