

WHAT CAN THE BLOOD TELL US ABOUT FOOD AND HEALTH?

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METABOLISM

Chemical processes within the body that keep an organism alive. These processes either use or create energy. Breaking down food into its chemical building blocks is one part of metabolism. When we eat, foods are broken down into smaller parts by the body. These smaller parts are called metabolites. Depending on the foods we eat, different metabolites enter the body. Microbes living in the gut can also take part in making metabolites. Metabolites from food or microbes can both appear in the blood. Studying blood metabolites could tell us what kinds of foods people generally eat or how healthy they are. To find out how eating different foods changes blood metabolites, we collected results from many previous experiments. We found that studying blood metabolites can tell us how food affects people's bodies. Interestingly, we also found that these effects appear to be different for each person.

INTRODUCTION

The chemical processes that happen in our bodies to keep us alive are collectively called **metabolism**. The fuel for these processes primarily

METABOLITES

Chemical building block of food. Metabolites can be produced by the body or the gut microorganisms, and they can be converted from one form to another.

MICROBES

Tiny microorganisms, like bacteria, viruses and some fungi, that cannot be seen with the naked eye.

GUT MICROBIOTA

The total community of microorganisms (microbes) living in the gut.

Figure 1

Metabolites from food are broken down by the digestive system and transported to other body parts. In the intestines, leftovers are eaten by gut microbes, and the remainder of the waste is flushed down the toilet. Blue arrows show the flow of metabolites and red arrows show the flow of the leftovers. comes from the foods we eat. After food enters the mouth, many things happen. In the mouth, food is chewed up into a paste-like form; then, it travels through the digestive system. As it travels along, the food is broken down into small pieces, called **metabolites**. When the metabolites arrive in the small intestine, which is toward the end of the digestive tract, they are transported into the blood. The blood delivers the metabolites to the rest of the body and its organs. The leftover food that we cannot break down then reaches the large intestine, which is the home to many gut **microbes**. The community of gut microbes, which is called the **gut microbiota**, helps us to break down the leftover food into smaller pieces. They eat a bit, but they return the rest to us. We can absorb some of the metabolites created by the gut microbes. We get rid of the leftover food that we do not need when we go to the toilet (Figure 1).

Because one important mission of the blood is to feed the rest of the body, the blood contains a lot of metabolites. These metabolites come directly from food or are created as food is processed through the digestive system. If we measure metabolites in people's blood after they eat specific foods, these measurements can give us information about how healthy the people are or which foods they ate. We can also get information about the gut microbiota, including which organisms live in the gut and how they change the metabolites.

WE ARE ALL UNIQUE, INCLUDING THE WAY WE DIGEST FOOD!

We are all unique. We have different colors of skin, eyes, and hair. Some of us play soccer, some dance ballet. Boys and girls are also different.

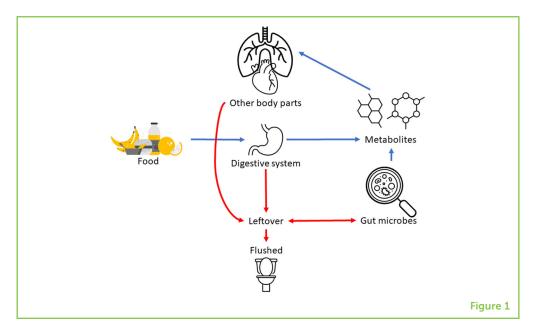
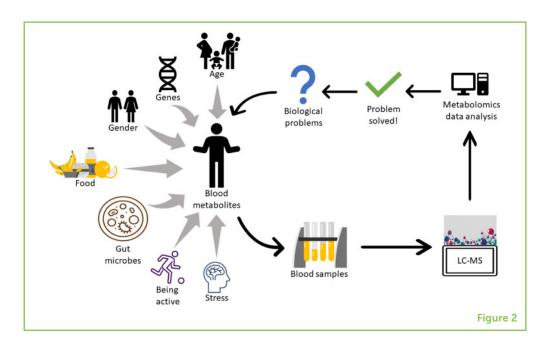


Figure 2

Metabolomics can be used to answer questions about what people eat and how the body manages metabolites. Many varied factors, shown on the left, affect how our bodies manage metabolites from the foods we eat. LC-MS is the scientific technique used to detect metabolites in blood samples. Metabolomics can help us answer many biological questions and can teach us about how every person's metabolism is unique.



Since we are so different on the outside, can we also assume that we have different processes inside our bodies?

We all eat different foods. Even within the same family, family members may have different favorite pizzas or soups. Maybe you like to eat chocolate or cakes, but your parents or grandparents may not enjoy those sweets as much anymore. They might not run and jump as much as you do, either! Different foods contain different types of metabolites. Therefore, when we eat different foods, we introduce many different metabolites into our bodies.

As we mentioned, the gut contains many microbes. Since the foods we eat vary a lot, the gut microbiota also varies a lot from one person to another. Your microbes are unique to you, just like your fingerprints. Your parents or siblings may have a similar set of microbes, but their gut microbiota will not look exactly the same as yours, even if you have a twin sibling [1]. Your unique set of gut microbes processes food uniquely within your gut.

If two people make cookies using different ingredients, methods, and toppings, they will end up baking different cookies. Similarly, because you are different from other people in how you look, your weight, your age, the foods you eat, the microbes in your gut, and how much exercise you get, the way you process your food may also be unique! Therefore, you and your siblings may have different chemical reactions going on in your bodies, even when you eat exactly the same foods [2]. Moreover, there are things we cannot see, like stress, that also cause differences in the way the body works. Since all these things affect how metabolites are created, you also have a unique set of metabolites (Figure 2)!

HOW DO WE STUDY METABOLITES?

What if we could check the metabolites inside each person? We would get information on how these metabolites differ from one person to another. Further, this information could give us some hints about the foods people eat, how their microbes act, and how their bodies process food. Well, we *can* do this!

First, we must take a small sample from the body. Depending on what we want to know, we can use samples of blood, urine, poo, or even exhaled air. We will focus on the blood because it carries the metabolites from the digestive system to feed the whole body. The blood sample is processed in the lab so that only the metabolites are left, in a clear liquid. This liquid can then be studied using a technique called **metabolomics**.

Metabolomics gives us information about the metabolites in a sample. Metabolomics uses a technique called **liquid chromatography–mass spectrometry** (**LC-MS**), which separates the metabolites from each other and shows how many metabolites are in each sample. Metabolomics analysis can give us a lot of information—it can tell us about hundreds or thousands of metabolites at the same time. We can then use this information to answer our research questions (Figure 2).

HOW DOES FOOD AFFECT OUR METABOLITES?

We wanted to know whether metabolomics studies of blood samples could tell us about how unique each person's metabolism is. We looked for past metabolomics experiments done by other researchers, to help us understand what has already been discovered and what we need to do next. We found 49 experiments reported in the last decade that studied levels of blood metabolites after various foods were eaten [3]. We grouped the studies based on how the metabolites are made, for example, whether they are produced by the body or by the gut microbiota. We were curious to see if the same groups of metabolites were generated by eating the same foods, or if one type of food consistently affected the same group of metabolites. We also wanted to see if metabolites were different between different groups of people. By examining these past studies, we learned at least three lessons.

First, different foods can affect our bodies differently. Though we may not realize it, food is complicated. How much oil we eat, whether we eat soy or dairy, or whether we eat more or less than usual activates different reactions in the body. As an example, having lots of dairy milk with breakfast increases different metabolites in the blood compared to a breakfast containing soy milk [4]. However, these results also depend on the people themselves. For example, people who were

METABOLOMICS

A technique to get information about many metabolites from a sample of blood or other bodily fluid or tissue.

LC-MS

A machine called liquid chromatography-mass spectrometry that helps us to study metabolites present in a sample. heavier seemed to show different reactions than people who were underweight [5].

Second, different types of metabolites can be affected by the same food. Let us take fish as an example. Fish is rich in protein. However, eating fish not only increases amino acids, the building blocks of protein, but also increase certain sugars in the body [6]. Also, similar metabolites can be affected by different foods. For example, the same metabolites changed after people ate soy, milk, meat, or whole grains, even though these foods are quite different from each other [6–8].

Lastly, the work of the gut microbiota plays an important role. In the experiments we compiled, almost all the foods investigated changed the metabolites produced by gut microbes. Some metabolites seemed to be found more often in healthy people than in people who were not well. On the other hand, other metabolites were found only in people with certain illnesses. We do not know yet if having a particular gut microbiota makes a person healthier or if the opposite is true—if healthy people tend to grow a different gut microbiota than people who are unwell. We need to do further research to figure this out.

CONCLUSION

Metabolomics can provide researchers with information about blood metabolites. These metabolites can tell us many things because they are affected by our body shape, age, and what we eat. Metabolites can also tell us about other processes happening in the body, like what the gut microbes are doing. By studying what other researchers have done, we learned that similar metabolites can be affected by different foods. Conversely, different groups of metabolites can be affected by the same foods. Based on these lessons, we think that, in the future, metabolomics could be used to find out how the foods we eat are related to health. This information could help us to better understand how and why people react differently to the same foods. Since we still do not know what causes these differences, further research is needed. Hopefully someday we will be able to use metabolomics to find which combinations of foods work best for each individual, so that we can all choose foods that help our unique metabolisms to work properly and keep us healthy.

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REFERENCES

- Turnbaugh, P. J., Hamady, M., Yatsunenko, T., Cantarel, B. L., Duncan, A., Ley, R. E., et al. 2009. A core gut microbiome in obese and lean twins. *Nature*. 457:480–4. doi: 10.1038/nature07540
- Johnson, A. J., Vangay, P., Al-Ghalith, G. A., Hillmann, B. M., Ward, T. L., Shields-Cutler, R. R., et al. 2019. Daily sampling reveals personalized diet-microbiome associations in humans. *Cell Host Microbe*. 25:789–802.e5. doi: 10.1016/j.chom.2019.05.005
- Noerman, S., Kolehmainen, M., and Hanhineva, K. 2020. Profiling of endogenous and gut microbial metabolites to indicate metabotype-specific dietary responses: a systematic review. *Adv. Nutr.* 11:1237–54. doi: 10.1093/advances/nmaa031
- 4. Meikle, P. J., Barlow, C. K., Mellett, N. A., Mundra, P. A., Bonham, M. P., Larsen, A., et al. 2015. Postprandial plasma phospholipids in men are influenced by the source of dietary fat. *J. Nutr.* 145:2012–8. doi: 10.3945/jn.115.210104
- Morio, B., Comte, B., Martin, J.-F., Chanseaume, E., Alligier, M., Junot, C., et al. 2015. Metabolomics reveals differential metabolic adjustments of normal and overweight subjects during overfeeding. *Metabolomics*. 11:920–38. doi: 10.1007/s11306-014-0750-y
- Tovar, J., de Mello, V. D., Nilsson, A., Johansson, M., Paananen, J., Lehtonen, M., et al. 2017. Reduction in cardiometabolic risk factors by a multifunctional diet is mediated via several branches of metabolism as evidenced by nontargeted metabolite profiling approach. *Mol. Nutr. Food Res.* 61:1600552. doi: 10.1002/mnfr.201600552
- Poesen, R., Mutsaers, H. A. M., Windey, K., van den Broek, P. H., Verweij, V., Augustijns, P., et al. 2015. The influence of dietary protein intake on mammalian tryptophan and phenolic metabolites. *PLoS ONE*. 10:e0140820. doi: 10.1371/ journal.pone.0140820
- Wallace, M., Green, C. R., Roberts, L. S., Lee, Y. M., McCarville, J. L., Sanchez-Gurmaches, J., et al. 2018. Enzyme promiscuity drives branched-chain fatty acid synthesis in adipose tissues. *Nat. Chem. Biol.* 14:1021–31. doi: 10.1038 /s41589-018-0132-2

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I love playing piano and drawing. My favorite sports are football and badminton. I love to hang out with my friends and family. I like to explore new things.

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I am professor at the research area "Food and Health" that I approach from the view of nutrition at the Institute of Public Health and Clinical Nutrition, University of Eastern Finland. My research interest is in the health effects of diets, foods, and food components with special focus on gut-mediated effects, such as digestion, inflammation, and microbiome interaction. In my free time I enjoy trailrunning with









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I am professor at Food Chemistry and Food Development unit at University of Turku. I completed Ph.D., in biotechnology at the University of Kuopio 2008. Since 2014 I have been the principal investigator in food and nutritional metabolomics research group, where we have focused on studying why and how different foods have different effects on our body and health. A special focus in our research is on the role of the small bugs in our intestine, the gut microbiota, and the favorite tool in our studies is the metabolomics analysis.

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