'You are what you eat,' and now researchers know exactly what you're eating

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An international team of scientists, led by researchers at University of California San Diego, report a new method called untargeted metabolomics to identify the vast number of molecules derived from

food that were previously unidentified, but that appear in our blood and our stool.

The method, described in the July 7, 2022 issue of *Nature Biotechnology*, matched all of the products of metabolism in a specimen to large databases of samples where chemical inventories were available, providing an unprecedented catalog of the molecule signatures created by consuming food or by processing it in our gut.

The authors said that, used broadly, the new approach could dramatically expand understanding of the sources of chemicals in many kinds of human, animal and environmental samples.

"Untargeted mass spectrometry is a very sensitive technique that allows for the detection of hundreds to thousands of molecules that can now be used to create a diet profile of individuals," said co-corresponding author Pieter Dorrestein, Ph.D., director of the Collaborative Mass Spectrometry Innovation Center at Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California San Diego.

"The expanded ability to understand how what we eat translates into products and byproducts of metabolism has direct implications for human health. We can now use this approach to obtain diet information empirically and understand relationships to clinical outcomes. It is now possible to link molecules in diet to health outcomes not one at a time but all at once, which has not been possible before."

Metabolomics involves the comprehensive measurement of all metabolites in a biological specimen. Metabolites are the substances, usually small molecules, made or used when an organism breaks down food, drugs, chemicals or its own tissues. They are the products of metabolism. The study also used a related technique, metagenomics, to measure genetic material in biological samples and characterize

microbes present.

Current metabolomics studies annotate or identify only 10 percent of molecular features in sampled specimens, leaving 90 percent of the material unknown. The new approach uses reference-data-driven (RDD) analysis to match metabolomics data derived from tandem mass spectrometry or MS/MS (an analytical tool that measures molecular weight using two analyzers instead of one) against metadata-annotated data is a pseudo-MS/MS reference library.

Essentially, each molecule is stripped of electrons to make it charged. The charged ion is weighed using a very sensitive scale, then smashed into pieces and those pieces weighed, creating a unique fingerprint for each molecule.

These collections of pieces or "fragmentation spectra" can be matched between the sample being analyzed and a reference database. However, until now the process has been very challenging.

In the new work, researchers investigated thousands of foods contributed by people around the world in the Global FoodOmics initiative launched at UC San Diego seven years ago, building on the success of the citizen-science American Gut Project/The Microsetta Initiative. The scientists increased their data output more than five-old over conventional techniques. Most importantly, the new method allowed untargeted metabolomics to be used to determine the diet based on a stool or blood sample.

The authors said RDD analysis allowed them to parse dietary patterns (vegan versus omnivore, for example) and consumption of specific foods and more generally, match the data against any existing reference databases.

"This advance is crucial because traditional methods for measuring diet, such as food diaries or food frequency questionnaires, are a pain to fill out and very hard to do accurately," said co-corresponding author Rob Knight, Ph.D., director of the Center for Microbiome Innovation at UC San Diego.

"The potential to read out diet from a sample directly has huge implications for research in populations like people with Alzheimer's Disease, who may not be able to remember or explain what they ate. And in wildlife conservation applications. Good luck getting a cheetah or a gorilla, to name just two species out of the hundreds we're studying, to fill out a food diary."

Of particular interest, said Dorrestein and Knight, were the large improvements in how many of the molecules in blood or stool that could be explained when food items were matched to population, such as matching food from Italy to people from the Cilento peninsula where UC San Diego scientists are collaborating on a study of centenarians.

"This really shows how important it will be to get both food specimens and clinical samples from people around the world in order to understand how our molecules and microbes work together to improve or degrade our health based on the diets we eat," said Knight.

"This study also points the way toward using RDD to explain the dark matter in our metabolome," added Dorrestein, "not only in terms of diet, but in exposures to chemicals from the clothes we wear, the medications we take, the beauty products we apply and the environments we are exposed to. It will truly let us explore the chemical connections between ourselves and the world we inhabit."

More information: Rob Knight, Enhancing untargeted metabolomics using metadata-based source annotation, *Nature Biotechnology* (2022).

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