How milk does an animal body good

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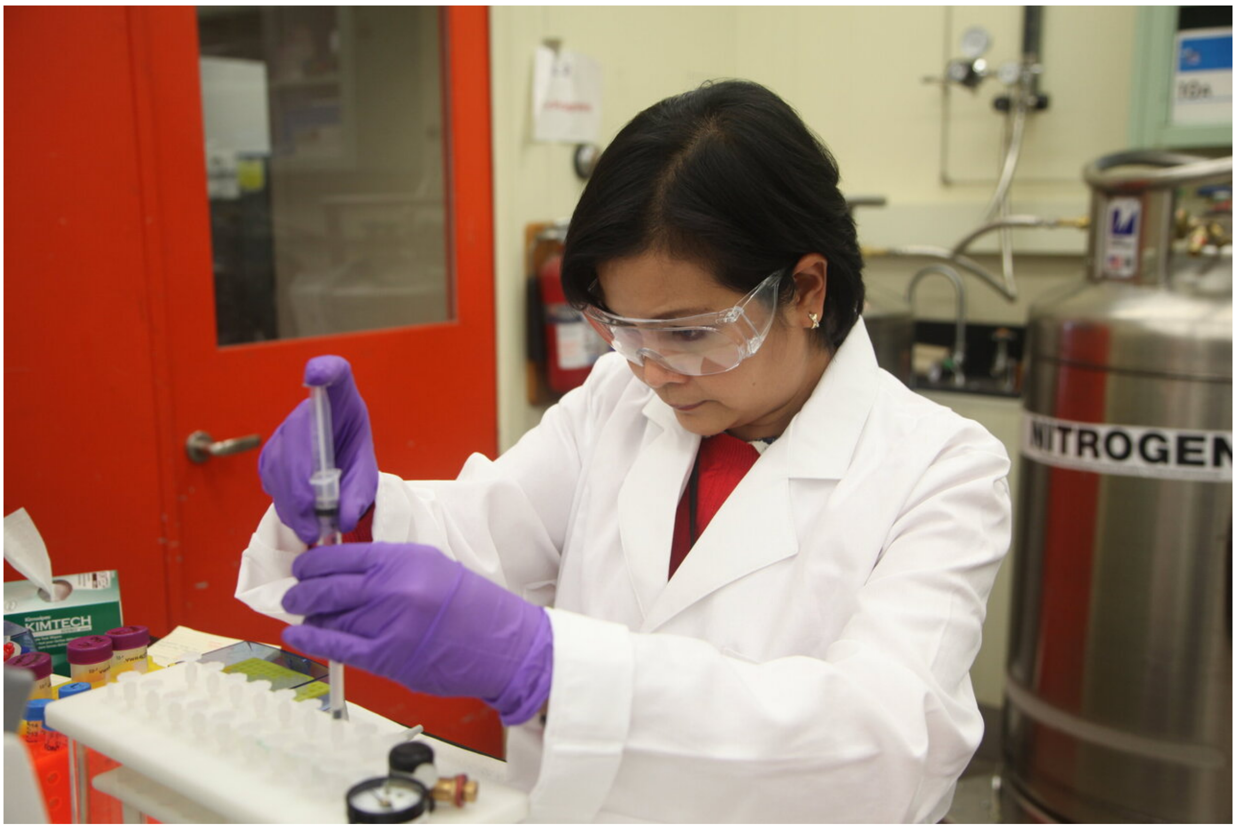

NIST chemist Connie Remoroza in her lab, working to prepare a milk sample from the National Zoo for ionization in the mass spectrometer. Credit: R. Press/NIST

It has been called the world's most perfect food, and there's unequivocal evidence that it can fight off disease and build better baby brains. But even after decades of research, very little is known about how breast milk does its work. To help complete the puzzle, chemists at the National Institute of Standards and Technology (NIST) are building a library to catalog important parts of this amazing and sometimes mysterious body fluid.

"We want to find as many details as we can about milk because it is so important, but so little is known about its chemistry," says Connie Remoroza, a chemist who leads the research project at NIST.

Remoroza has been working with others in NIST's Mass Spectrometry Data Center (MSDC) to analyze some of milk's unique sugars, known as oligosaccharides. Oligosaccharides are carbohydrates. They usually include anywhere from three to 10 simple sugars such as glucose, linked together by chemical bonds. Scientists are learning that they play a role in baby brain development and increased immunity to infection.

In addition to their presence in milk, oligosaccharides occur in many plants, such as legumes, onions, wheat and asparagus. A large majority of them are not digested or absorbed by the body when eaten; instead they end up in the colon. What role they play there is still largely unknown, although many refer to them as prebiotic, because it is assumed that they encourage the growth of good bacteria, which in turn creates a healthy, functional microbiome for the body. Some research has also shown that prebiotics like oligosaccharides could be aiding the absorption of calcium, magnesium and other minerals in the human gut.

The NIST library that Remoroza and her fellow scientists are building will act as a reference for those who want to do further work on the topic to find definitive answers to these digestive uncertainties.

In the summer of 2018, Remoroza and her colleagues documented 74 unique oligosaccharides in NIST's Standard Reference Material (SRM) 1953. SRM 1953 was acquired in conjunction with the Centers for

Disease Control and includes pooled milk samples from 100 breastfeeding mothers, purchased frozen from six different milk banks in the U.S. in 2006. Chemists often use it to determine if methods for finding environmental contaminants like polychlorinated biphenyl (PCBs) and pesticides are effective. Twelve of the oligosaccharides documented by Remoroza had not been found in human milk before.

The discoveries were made with a mass spectrometer, an instrument used to measure the chemical structure of molecules and chemical compounds. Chemists use those measurements to chart out "mass spectra," which are like unique fingerprints that can help identify the composition of the original sample.

Connie Remoroza and Mike Power discuss breast milk samples at the National Zoo's milk repository. Credit: R. Press/NIST

Over the last decade or so, liquid chromatography and mass spectrometry has increasingly been used to analyze carbohydrates, including oligosaccharides, to find their unique fingerprints. Measuring carbohydrates can be more challenging than measuring the structure of other things, though, and consequently little is known about them. By building a library, NIST is filling a large data gap.

"Once this information is published, anyone will be able to use it for all kinds of research purposes," says Stephen Stein, lead scientist in the MSDC.

The NIST team has recently been turning its attention to other types of mammalian milk. First, Remoroza catalogued the oligosaccharides of domestic animals, such as cows and goats. Then one day, she sat in front of a modest spreadsheet she'd created to detail which types of milk had already been researched by chemists using mass spectrometers like the one in her lab. She wondered what she could find in the milk of bears, platypuses and apes. It dawned on her that one of the world's premier research zoos was just a few miles away, on Connecticut Avenue in Washington, D.C. She wondered: Do they have milk to share with us?

A quick email confirmed that the scientists working at the Smithsonian's National Zoo and Conservation Biology Institute had indeed amassed quite an unusual collection of exotic mammal milk. And they were just as excited about oligosaccharides in the milk as she was. Although the zoo has access to lots of animal milks and is currently storing more than 15,000 samples, it lacks NIST's technical capabilities and the equipment needed to study those milks' molecules. A partnership was formed in December 2018.

"Mammals are the only big set of animals which are all defined by the fact that their females produce a substance from their own body to feed their offspring," says Mike Power, one of the zoo's animal scientists who has been working with Remoroza. "Everything from an armadillo to an elephant to a human being."

While they all produce milk, the contents of each type can vary widely. Elephants and rhinos have very different milks, for example, even though they live in the same habitat and live much the same lifestyle.

The milks of our closest relatives, the apes, are similar to ours, although human milk does have about twice the fat. But recent technological advances have helped us see further into the fluid for more information. Scientists recently learned that oligosaccharides tend to be more diverse and more plentiful in humans than they are in other animals—even the apes. About 20 percent of the sugar in human milk is in oligosaccharides. This is in sharp contrast to gorilla milk, where the share is closer to 5 percent.

Power thinks these details may help us understand evolution.

To safely transport the animal milk samples back to the NIST campus in Gaithersburg, Remoroza packed them carefully in a polystyrene-lined box with several dry ice packs. Credit: R. Press/NIST

"People talk about milk being the perfect food. I'd say it's the best evolved food, but it's not perfect," he says. Knowing more about the oligosaccharides will tell us about human milk now and how it is important, and not important.

"It seems to be mostly immune function. Which makes a hell of a lot of sense when you start thinking about how we changed our environment." Unlike apes, humans began raising crops, and raising domestic animals. Eventually, humans also began using manure to fertilize crops, which in turn could pass on new, virulent diseases like swine flu. The exposure likely demanded more of human immune systems, including milk, Power says.

The more details Remoroza can provide on the milk, the more likely researchers are to build better substitutes for it. This could help veterinarians, conservation biologists and dieticians at zoos, who often must feed a baby when the mother won't (or can't) provide, such as the famous example of Fiona the Hippo at the Cincinnati Zoo in 2017. When the little hippo was born and unable to get what she needed, Power and his team at the National Zoo were called upon to create as close a duplicate to her mother's own milk as possible.

NIST's oligosaccharide library could help in other similar situations in the future. But it could also aid in the development of better baby formulas for humans.

Remoroza is hoping to access the zoo's frozen resources to study milk from a wide variety of animals, such as okapis, elephants, gorillas, and maybe even anteaters. She's starting with African lions, however, because she realized very little research had been done on carnivores and the zoo has lots of African lion milk to share for the library.

The oligosaccharide library is available free on the NIST website and will be updated as new data becomes available.

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