Baby's First Microbiome

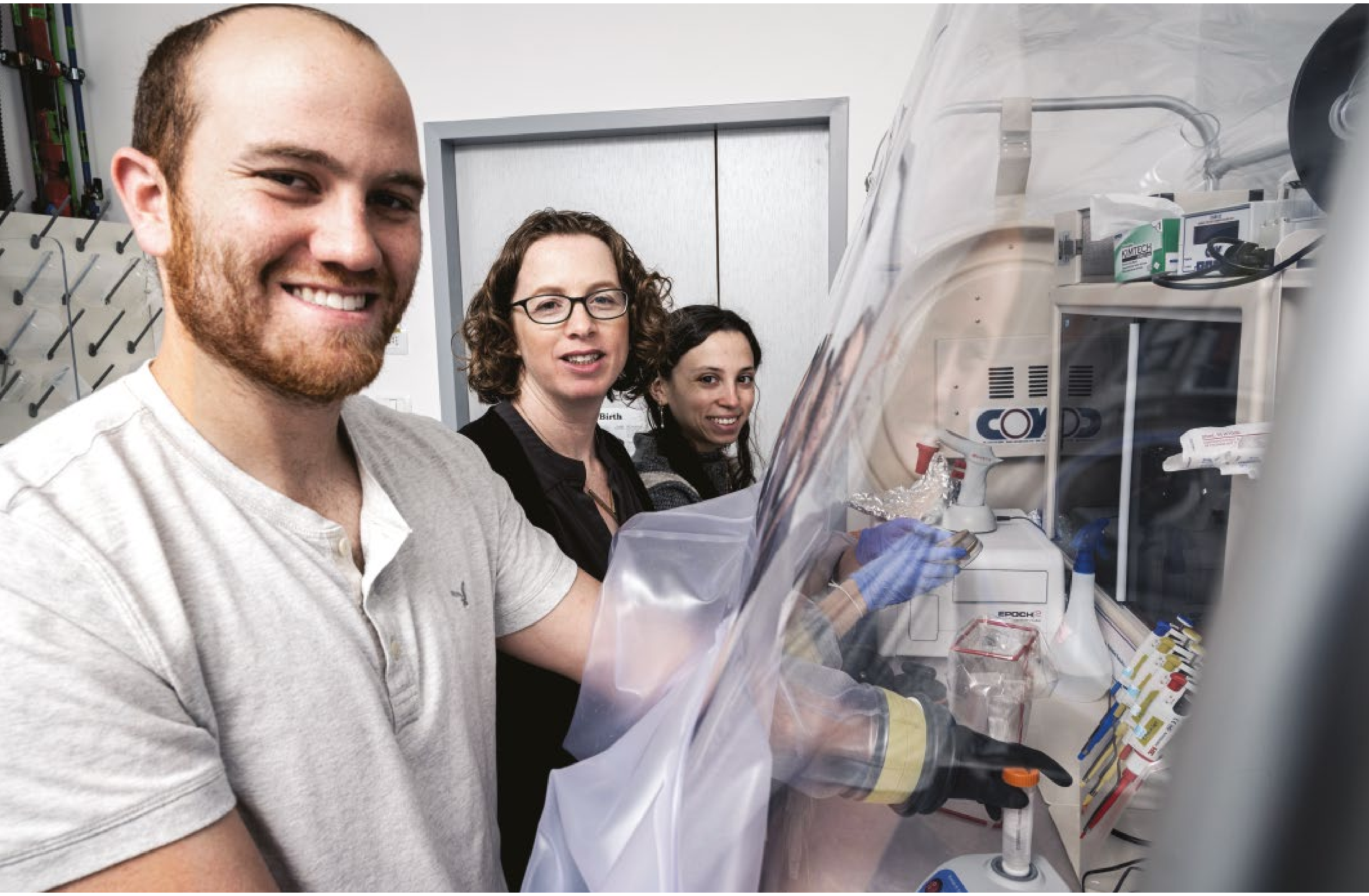
An infant's gut is one of the keys to developmental health, and Moran Yassour wants to decode the role that microbes play

Computational biologist Moran Yassour, an Azrieli Early Career Faculty Fellow at the Hebrew University of Jerusalem, researches a vital but often overlooked aspect of human development: the newborn gut.

More specifically, she is studying how the gut is colonized by microbes, how sugars found only in breastmilk nourish beneficial microbes, and how the establishment of this critical community of microorganisms — known as the human gut microbiome — affects the health of not only babies but children and adults too.

There is a bustling assemblage of bacteria, archaea, fungi and viruses within our gastrointestinal tract, and this microbiome is one of the keys to well-being. The important roles that these microbes play has become increasingly evident in the fifteen or so years

By Anne Shibata Casselman
Photographs by Ariel van Straten



The microbial signatures in the guts of infants borne vaginally and by cesarian section differ and change over time. The differences are so pronounced that by analyzing a stool sample, Moran Yassour can determine how a baby was born. By studying changes in this community of microbes, she aims to address questions such as why infants born by caesarian have a greater chance of developing autoimmune diseases.

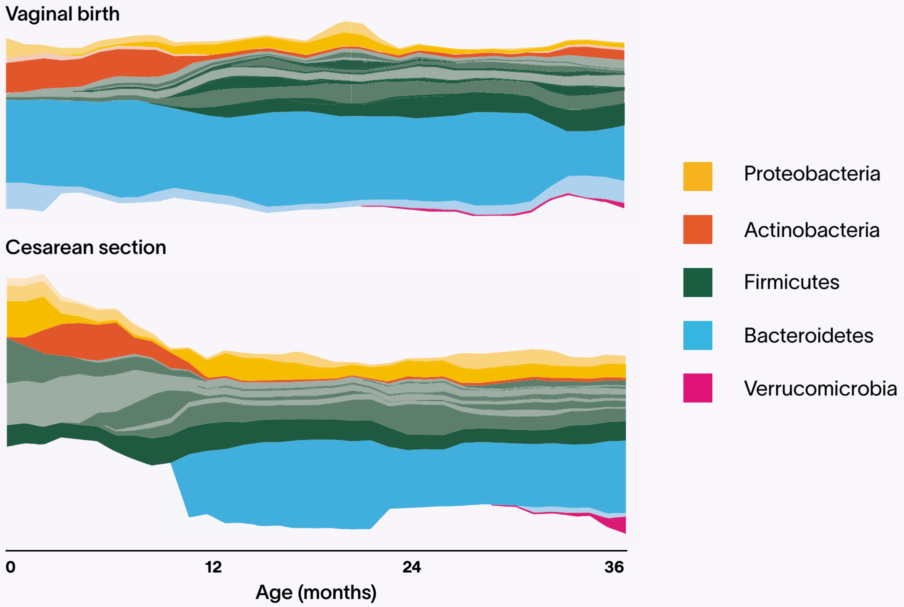


DIAGRAM BY DALBERT B. VILARINO; SOURCE: MORAN YASSOUR

Autoimmune disorders arise when the immune system incorrectly identifies elements within our bodies as foe. A healthy gut microbiome appears to be an important training ground for early lessons that lessen the chance of developing an autoimmune disorder.

Moran Yassour (middle) with students Nadav Moriel and Sivan Kijner in her lab, where their research is deepening our understanding of the infant gut microbiome.

ILLUSTRATION COURTESY PEANUTS CREATIVE STUDIO

since genetic sequencing began providing a more detailed picture of what's happening inside our bodies. The microbiome is home to trillions of microbes and it is proving to be as critical to development as any organ. It is implicated in a long list of ailments, from inflammatory bowel disease and type 2 diabetes to colorectal cancer and rheumatoid arthritis, among others. The microbiome helps regulate everything from our metabolism and sleep patterns to our immune system, the majority of which is found in the gut. Autoimmune disorders arise when the immune system incorrectly identifies elements within our bodies as foe; a healthy gut microbiome appears to be an important training ground for early lessons that lessen the chance of developing an autoimmune disorder.

In other words, the formation of this community of microorganisms during infancy has lifelong consequences. Despite this great impact, however, very little is known about how microbes colonize the gut during infancy or how the composition of the microbiome affects pediatric disease. Yassour, who is cross-appointed to the Faculty of Medicine and the School of Computer Science and Engineering, explores this scientifically rich niche at the Hebrew University, where she earned all three of her degrees and to which she returned in 2018 after a postdoctoral fellowship at the Broad Institute of MIT and Harvard. While in Boston, she found herself wondering about the factors contributing to differences in infant gut microbes. "Being a mother myself," she says, "it intrigued me."

Today, Yassour works in her lab with a dozen or so students, from undergraduates to PhDs, with backgrounds ranging from microbiology and medicine to pure computer science. Together, they grow bacterial cell cultures in anaerobic environments that simulate the infant gut, sequence bacterial DNA from stool samples and use machine learning algorithms to map out not only what type of microbes inhabit our guts, but also the specific strains and their functionality, and how they may play a role in pediatric health.

Yassour has made significant progress in the eight years since starting her research in this field. She has debunked the belief that the vaginal microbiome seeds the infant gut microbiome during birth (the source appears to be rectal) and traced mother-to-child transmission of the microbes that colonize the infant gut. She has also continued to lay the groundwork for more ambitious and applied work. Eventually, thanks to her research, infant formula could better mimic breastmilk's ability to nurture healthy children, and lifesaving caesarean deliveries won't deny babies the microbial boost experienced from vaginal births.

"We still need to answer many of the basic science questions," says Yassour, "before we can move on to address the big important ones." Infants born by caesarian, for example, have a greater chance of developing autoimmune diseases than those who are born vaginally. Yassour wants to find out whether differences in their microbiomes are at the root of this disparity. At six months of age, a child born by caesarian has a different microbial signature in their gut than one who is born vaginally. The signs are so strong that if you were to give her a stool sample from an infant's diaper, she could tell you how that baby was born with 80 per cent accuracy. Breastfed infants also have unique signatures in their gut microbes compared with formula-fed infants.

Yassour is interested in teasing apart the precise impact of these variations. One way to do this is by decoding the microbial make-up of stool samples collected from individuals across multiple points in their early lives. "We can collect longitudinal cohorts of infants or older children that have a medical condition that is associated with immunity early on in life, profile their microbiome and search for differential features, such as specific microbial taxa," she says. She is collaborating with researchers at Massachusetts General Hospital in Boston to study an allergy that some infants develop to the proteins in cow's milk. Although the allergy resolves on its own, children who develop it have a higher chance of developing life-threatening food allergies, such as to nuts or shellfish, later in life.

Yassour and her colleagues are analyzing stool samples from ninety babies who developed this allergy during the first year of their lives and ninety who did not to compare their gut microbiomes. "We find some overall differences in microbial diversity between the groups," she says of their findings so far, "and also identify bacterial species that have a higher abundance in one group than the other." Moreover, the researchers found differences during the period that the allergy presents and after it resolves, and they are examining the specific bacteria at play.

Human breastmilk is another key to fostering beneficial gut microbes in infants. To better understand its impact, Yassour must first clarify the effect that the complex sugars found only in breastmilk have on the infant gut microbiome. These sugars, known as human milk oligosaccharides (HMOs), are the third most common component of breastmilk. A mother's body invests significant energy making these complex sugars, which can only be broken down by the beneficial microbes in her baby's gastrointestinal tract. These HMOs seem to act as a baby's first prebiotic, a food that will encourage the growth of the microbes that use it as an energy source (compared to probiotics, which involve administering live microorganisms).

There are between fifty to two hundred different structures of HMOs. Yassour and her team are currently feeding various HMOs to bacteria collected from the infant gut to determine which bacteria thrive on which HMOs. From there they hope to find the simplest combination of HMOs that best mimics a "universal breastmilk." Yassour is quick to aver that she is not taking sides in the formula versus breastfeeding conversation. "Infant formula is really important," she says. "We all agree that its intention is to mimic breastmilk, so let's think about how we can mimic it in all possible ways." At the same time, Yassour is thinking about myriad ways to gain a better understanding of the infant gut microbiome and its long-term health implications. ▲●■

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Yassour (facing page), who grows bacterial cell cultures in her lab that simulate the infant gut and performs computational analyses, gathers with students (above, left to right) Netta Barak, Nadav Moriel, Ehud Dahan, Chiara Mazzoni, Sivan Kijner and Lior Merav.