

Delivering inventions for healthy pregnancies

α-DEFENSIN is used to evaluate microbiome health and **SMART TAPE** remotely monitors uterine contractions.

Researchers aiming to improve healthy birth outcomes in Japan have identified a compound that is a practical indicator of microbiome health and invented a smart tape to remotely monitor mothers for signs of unusual contractions. “We are beginning to see that babies inherit the microbiome and epigenome of their mother at birth,” explains Kiminori Nakamura, from Hokkaido University’s Faculty of Advanced Life Science.

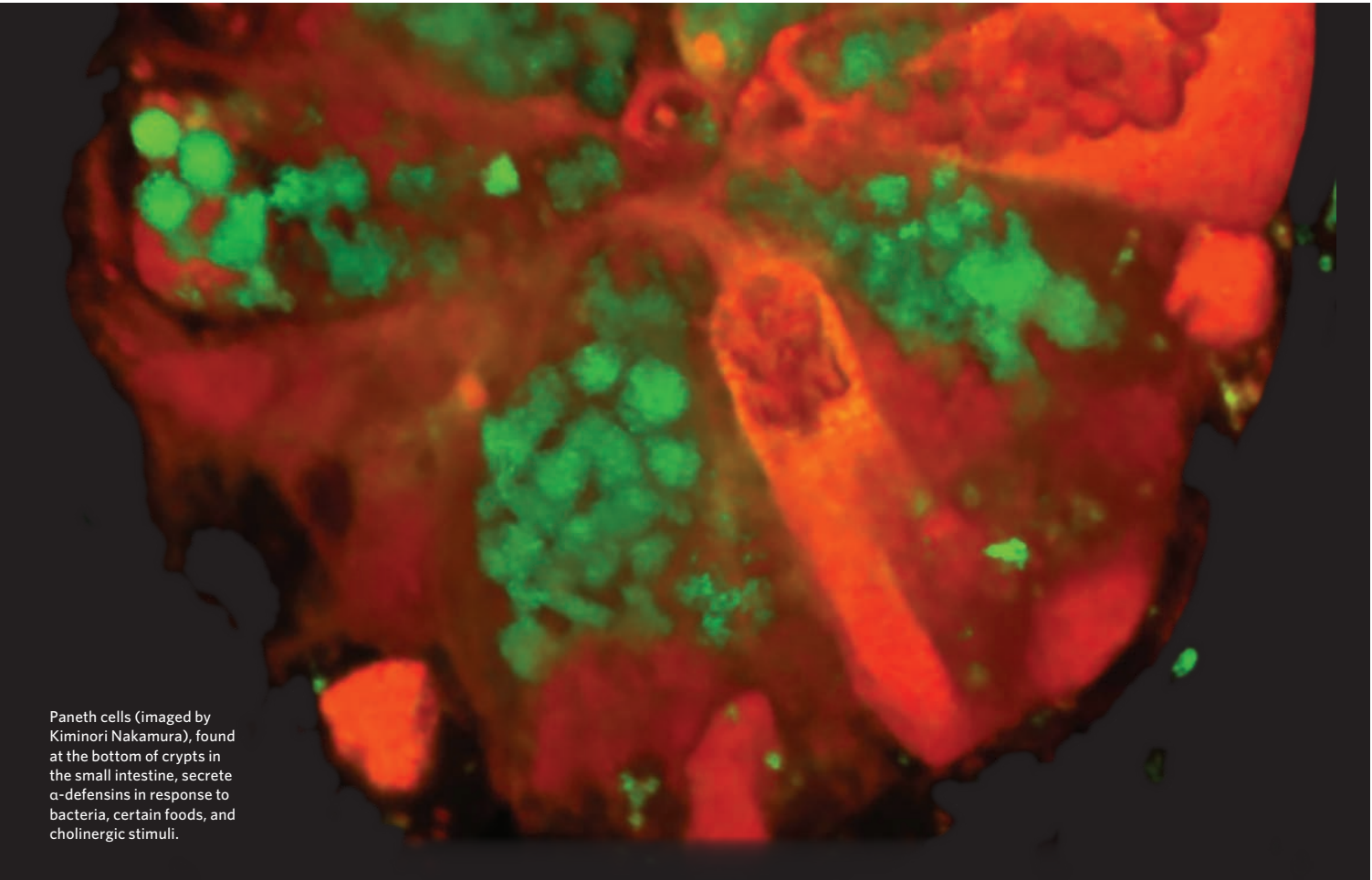
However, the average body-mass index of pregnant mothers in Japan is decreasing, and the microbiomes that mothers pass on to their babies appear to be changing. Nakamura, along with Hokkaido University researchers, Tokiyoshi Ayabe and Shinji Nakaoka, is investigating the link between a mother’s microbiome and the likelihood of low-weight births, as well as the health of low birth weight babies over time.

The project, run through Hokkaido University’s Center of Innovation, aims to reduce the rate of low-weight births in Iwamizawa, Hokkaido, the city with Japan’s second lowest birth rate.

PRACTICAL PROXY
α-Defensin, a compound secreted from cells in the small intestine called Paneth cells, is key to evaluating a mother and child’s microbiome, says Ayabe, a leading figure in inflammatory bowel disease. “These cells were largely ignored in the research world 30 years ago, but are garnering much attention today for their role in innate immunity and regulating gut flora,” he says.

Recent studies find that α-defensin plays a significant role in controlling microbiome diversity; in 2020, Ayabe and Nakamura found that mice with Crohn’s disease released a deformed version of α-defensin, which led to an imbalance in gut flora. The compound serves as a potent microbicide against pathogens, while maintaining symbiotic bacteria.

Many diseases like obesity, allergies, cancer, and lifestyle diseases are associated with low microbiome diversity. Because of this, the team has started to position α-defensin as a proxy for evaluating microbiome health. “A ‘good’ microbiome can look very different between people. Just because a person



Paneth cells (imaged by Kiminori Nakamura), found at the bottom of crypts in the small intestine, secrete α-defensins in response to bacteria, certain foods, and cholinergic stimuli.

doesn’t have the same microbial profile as another healthy person, it does not mean that they are unhealthy,” says Nakaoka, who performs big data analyses in the project. “With the extreme variability that we see, it becomes difficult to identify similarities.”

GUT DIVERSITY CONTROL
Ayabe emphasizes that α-defensin, secreted from the body’s own cells, plays a role distinct from prebiotics and probiotics. “α-Defensins are about leveraging a mechanism programmed into the body’s own cells, rather than about feeding or consuming microbes, as is the case with prebiotics

α-DEFENSINS COULD BE USED AS PROXIES FOR MICROBIOME HEALTH

and probiotics. Although prebiotics and probiotics are important in themselves, α-defensins show us that the body’s innate mechanism for controlling microbiome diversity is also a crucial element to consider,” he says.

In a world first, Nakamura developed a technology to measure α-defensins from human stool samples. With this, they continue to

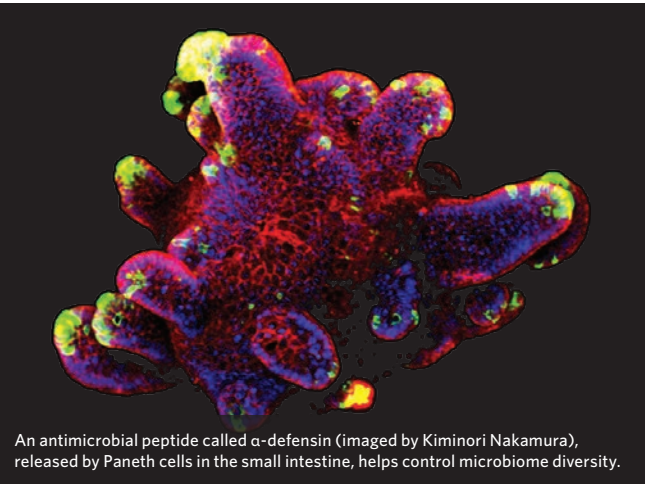
find associations between α-defensin, metagenomes, metabolites, and metabolomes from thousands of samples collected from mothers and their children over several years.

In addition, Nakaoka’s analyses are bringing to light the types of foods that stimulate Paneth cells into secreting α-defensin. “Some ingredients that we are examining are those that our business collaborators provide, while others are ingredients in Japan’s traditional herbal kampo medicine,” explains Nakamura. “In 2019, our group found that leucine – a type of amino acid – increases α-defensin secretion in mice.

The picture for humans, however, is turning out to be more sophisticated.” Eventually they hope these findings will serve as a basis for personalized diet recommendations in preventing low-weight births.

SMART-TAPE MONITORING
Closely linked to low birth weights are premature births. To allow the remote detection of warning signals, Takeshi Umazume, of Hokkaido University Hospital, is developing a wearable device that detects uterine contractions.

The technology could prove particularly useful in rural Hokkaido, where pregnant



An antimicrobial peptide called α-defensin (imaged by Kiminori Nakamura), released by Paneth cells in the small intestine, helps control microbiome diversity.



Takeshi Umazume (pictured) of Hokkaido University Hospital is developing a wearable device that detects unusual uterine contractions remotely.

women from far away villages sometimes have to rent short-term accommodation in urban areas for months to be close to services as they prepare for delivery. For some, this means leaving their other children behind in the care of others for an extended period.

Umazume describes the new wearable device – designed in partnership with a tape manufacturer – as a tape with pressure sensors that mothers can attach themselves across the abdomen.

“When contractions suddenly become frequent, it’s a sign that labour is near. If this happens early, it can be an indicator that there is

inflammation in the uterus, and some women have to give birth early via a C-section,” says Umazume.

“Contractions are a simple signal that can tell us loads about an expecting mother’s state of health. With this tape, women can keep it on during the night, allowing us to monitor 24-7.” A corresponding smartphone app also records signals from the device, so that clinicians and mothers can receive alerts when labour is imminent. ■

