Microbes may play crucial role in human health

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> Few people today realise the critical importance of probiotics in maintaining health and well being; unpasteurized fermented products such as buttermilk, yoghurt and kefir are laden with health-giving living bacteria necessary for the balanced function of our bodies.

The average person's body contains about 100 trillion cells, but only one in ten is human!

The human cells that form our skin, eyes, ears, brain and every other part of our bodies are far outnumbered by those from microbes — primarily bacteria but also viruses, fungi and a panoply of other microorganisms.

That thought might make a lot of people lunge for the hand sanitizer, but that impulse may be exactly the wrong one. Researchers are amassing a growing body of evidence indicating that microbial ecosystemsplay crucial roles in keeping us healthy.

Moreover, scientists are becoming more convinced that modern trends — diet, antibiotics, obsession with cleanliness, Caesarean deliveries — are disrupting this delicate balance, contributing to some of the most perplexing ailments, including asthma, allergies, obesity, diabetes, autoimmune diseases, cancer and perhaps even autism.

"In terms of potential for human health, I would place it with stem cells as one of the two most promising areas of research at the moment," said Rob Knight of the University of Colorado. "We're seeing an unprecedented rate of discovery. Everywhere we look, microbes seem to be involved."

Equipped with super-fast new DNA decoders, scientists are accelerating the exploration of this realm at a molecular level, yielding provocative insights into how these microbial stowaways may wield far greater powers than previously appreciated in, paradoxically, making us human.

"The field has exploded," said Jeffrey I. Gordon of Washington University, who pioneered the exploration of humanity's microbial inhabitants, known as the "microbiome" or "microbiota." "People have this sense of wonderment about looking at themselves as a compilation of microbial and human parts."

Some equate these microbial inhabitants to a newly recognized organ. Acquired beginning at birth, this mass of fellow travelers may help steer normal development, molding immune systems and calibrating fundamental metabolic functions such as energy storage and consumption. There are even clues that they may help shape brain development, influencing behavior.

“The ‘human supraorganism’ is one term coined to describe the human host and all the attendant microorganisms,” said Lita M. Proctor, who leads the Human Microbiome Project at the National Institutes of Health, which is mapping this world. “There’s been a real revolution in thinking about what that means.”

Nurturing microbes

Investigators are trying to identify which organisms may truly be beneficial “probiotics” that people could take to help their health. Others are finding substances that people might ingest to nurture the good bugs. Drugs may mimic the helpful compounds that these organisms produce.

Doctors have even begun microbiota “transplants” to treat a host of illnesses, including a sometimes-devastating gastrointestinal infection called Clostridium difficile, digestive system ailments such as Crohn’s disease, colitis and irritable bowel disorder, and even, in a handful of cases, obesity and other afflictions, such as multiple sclerosis.

Many advocates of the research urge caution, noting that most of the work has involved laboratory animals or small numbers of patients, that many hypotheses remain far from proven and that nothing has zero risk.

“We have to be very careful in how we state what we know at the present time versus what we think might be true at this point,” said David A. Relman of Stanford University. “But it’s probably fair to say that our indigenous communities are more diverse, more complex and more intimately and intricately involved in our biology than we thought.”

Our inner microbes

Scientists have long known that many organisms evolved with humans and perform vital functions, digesting food, extracting crucial nutrients and fighting off disease-causing entities.

“We feed them and house them, and they perform certain metabolic functions for us that we have sort of contracted out,” said Martin J. Blaser of the New York University School of Medicine. “The homeboys protect their turf from invaders.”

But as microbiologists have begun scrutinizing these colonies, it has become clearer that they create carefully calibrated enterprises, with unique combinations inhabiting individual crevices and identifiable nuances from person to person.

“We just don’t pick up willy-nilly any microbe in the soil or air we encounter,” Relman said.

European scientists reported in April that people generally seem to have one of three basic combinations that may be as fundamentally important as, say, blood type.

The five-year, $175 million U.S. Human Microbiome Project is assembling an outline of a “healthy” microbiome by sampling the mouth, airway, skin, gut and urogenital tract of 300 healthy adults, as well as deciphering the genetic codes of 200 possibly key microbes.

Dozens of studies also are underway, including some in which children and adults, including twins, are repeatedly swabbed to gain insights into why one person gets tooth decay, asthma, ulcerative colitis or even cancer, and another doesn't.

"We're using microbes as markers for the onset of various diseases or progression of diseases," said Karen E. Nelson, who runs the J. Craig Venter Institute in Rockville. "We think we're going to have a huge impact on health."

One intriguing finding is that babies born through Caesarean section apparently miss out on acquiring their mothers' microbiota.

Birth, development, disease

"The birth canal is very heavily colonized by bacteria," said Maria Dominguez-Bello, a University of Puerto Rico biologist who has been studying microbiota around the world, including among isolated tribes in the Amazon. "We think that is not by chance."

The rising number of C-section babies denied this colonization, along with the casual use of antibiotics and other factors that can alter the microbiota, might help explain trends such as rising incidents of asthma and food allergies caused by misfiring immune systems. To explore this, researchers have begun following C-section babies, comparing their microbiomes and their health with babies delivered through the birth canal.

The interaction between the microbiota and the immune system may also play a role in other diseases in adults, including those caused at least in part by chronic inflammation from hyperactive immune systems.

"Gut bacteria have figured out a way to network with our immune system so it doesn't attack them," said Sarkis K. Mazmanian of the California Institute of Technology.

The microbiota apparently sends signals that dampen the "inflammatory response," a crucial defense also thought to play a role in a variety of diseases, including many forms of cancer, the "metabolic syndrome" caused by obesity, diabetes and heart disease.

The theory is that one reason some people may be prone to these diseases is that they are missing certain microbes. One anti-inflammatory compound produced by a bacterium appears to cure the equivalent of colitis and multiple sclerosis in mice, both of which are caused by misfiring immune systems, Mazmanian found.

Role in obesity?

Similarly, studies indicate that gut dwellers secrete messengers to cells lining the digestive tract to modulate key hormones, such as leptin and ghrelin, which are players in regulating metabolism, hunger and a sense of fullness.

Pregnant women often take antibiotics, and young children can get several rounds to fight ear and other infections, which can kill off these companions. Farmers commonly add antibiotics to animal feed to fatten their animals faster.

"We may have a generation of children growing up without the proper bacteria to regulate their leptin and ghrelin," Blaser said.

Obese people appear to have a distinctive mix of digestive bacteria that make them prone to weight gain. Thin mice get fatter when their microbiota is replaced with the microbes of obese animals.

“Our ancient microbiome is losing the equilibrium it used to have with the host — us — and that has profound physiological consequences,” said Blaser, who published his concerns in a paper in the journal Nature in August.

Microbes and the mind

Clues also are emerging about how microbes may affect the brain. Manipulating gut microbiomes of mice influences their anxiety and activity, Swedish researchers reported in January in the Proceedings of the National Academy of Sciences.

“This may have implications for new lines of thinking to address some of the psychiatric problems you see among humans,” said Sven Pettersson, a professor of host-microbial interaction at the Karolinska Institute. “Together with genetic susceptibility, this may influence what doctors classify as autism or ADHD.”

In another experiment involving mice, a Canadian-Irish team reported in August that bacteria in the gut appear to influence brain chemistry, and corresponding behaviors such as anxiety, stress and depression, via the vagus nerve.

“What we’ve shown is, you change behavior as well as make changes in the brain,” said John Bienenstock, director of the Brain-Body Institute at McMaster University. “Now we have direct proof how that happens. That’s why this is exciting.”

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