Researchers discover potential biomarker to detect 'bubble boy' disorder

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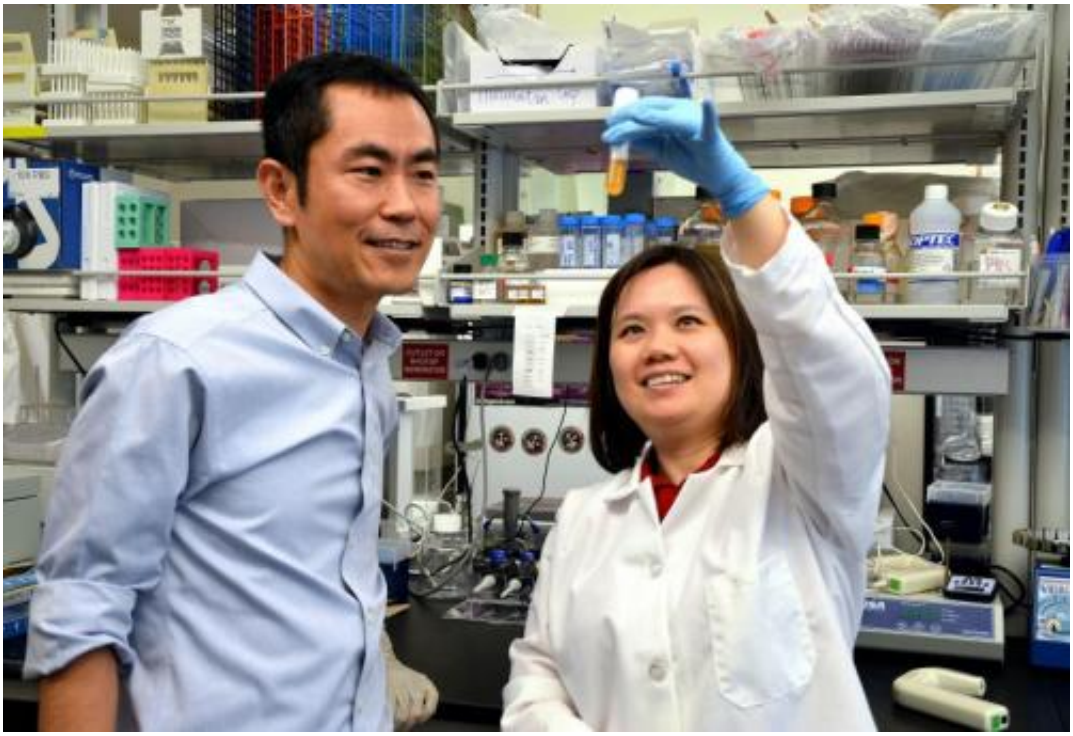

Xin M. Luo (right), an assistant professor of immunology in the Virginia-Maryland College of Veterinary Medicine, and Husen Zhang, a research assistant professor of Civil and Environmental Engineering, work to discover ways to detect a deadly childhood illness. Credit: Virginia Tech

Many people recognize "the bubble boy" as an unusual character from a "Seinfeld" episode or a John Travolta movie.

But in reality, a genetic disease called SCID, short for severe combined immunodeficiency, forces patients to breathe filtered air and avoid human contact because their bodies' natural defenses are too weak to fight germs.

Although it affects fewer than 2,000 new births each year worldwide, SCID is a cousin to acquired immune deficiency syndrome triggered by a human immunodeficiency virus—HIV/AIDS.

Now, using a mouse model, Virginia Tech researchers in the September issue of *The ISME Journal* describe a potential biomarker to detect SCID by analyzing for a microbe in the fecal matter of infants.

"If SCID is not detected, children cannot live past their first year," said Xin M. Luo, an assistant professor of immunology Virginia-Maryland College of Veterinary Medicine. "Now, we may have a noninvasive way to screen for this disease because this microbe may be present only in negligible amounts in healthy, young children. If larger populations of the microbe are present, quick examination is needed to prevent a potentially deadly emergency."

Luo, a faculty member in the Department of Biomedical Sciences and Pathobiology, worked with Husen Zhang, a research assistant professor in the Department of Civil and Environmental Engineering in the College of Engineering, to compare the gut microbes in healthy mice with those in mice with a defective immune system, both before and after weaning. They found that the defective mice had a greater supply of a particular microbe called *Akkermansia muciniphila*.

"This is also a human intestinal microbe," said Zhang, a microbial ecologist who performed the gene sequencing in partnership with the Virginia Bioinformatics Institute. "Although it is rather newly discovered, it has been there for a long time. Previous reports found that

the microbe increases with antibiotic use, indicating that it might thrive when other gut microbes don't survive a round of antibiotics."

When Luo performed bone marrow transplants on the defective mice to give them an adaptive immune system, the researchers found that this particular microbe returned to normal levels. The difference only occurs in younger mice and gradually subsides with age.

"This is an interesting finding because it means we can potentially screen for this microbe at an early age to find defects in the immune system," Luo said.

Although SCID affects less than 0.1 percent of the human population, the disease is typically fatal to children without diagnosis and treatment within their first year. Physicians have found success in treating the genetic disorder with bone marrow transplants.

The researchers are collaborating with a pediatrician to test samples from human infants and have filed a provisional patent for the biomarker screening. Joshua Sparks, a third-year medical student at the Virginia Tech Carilion School of Medicine, also assisted with the research as a part of his degree program.

Many researchers have looked into the impact of gut microbes on the immune system—with recent studies investigating the unintended effects of antibiotics on helpful bacteria or the use of probiotics to boost the immune system. But Luo and Zhang are among only a handful of researchers who have turned their attention in the opposite direction.

"There have been many studies recently on how gut microbes modulate the immune response, but we wanted to do the opposite" Luo said. "We are asking the question, 'How does our immune system affect bacteria in the gut?' "

More information: The study is called "Host adaptive immunity alters gut microbiota."

Provided by Virginia Tech