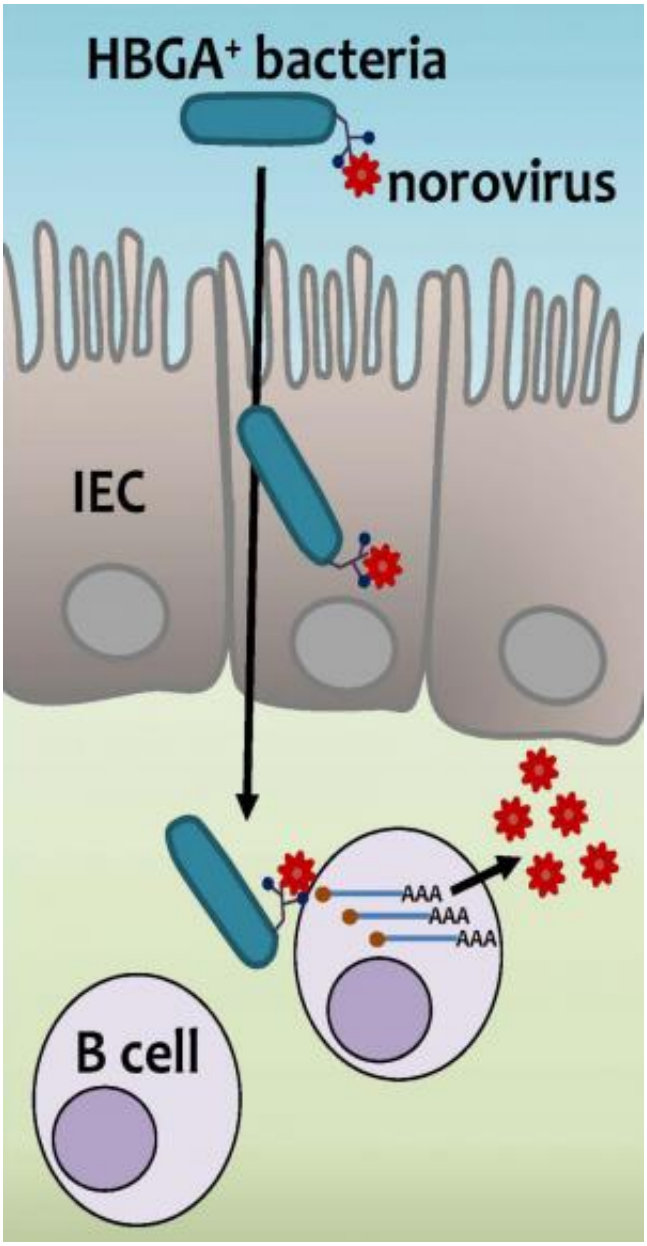
Researchers grow norovirus in human cells

November 7 2014, by Morgan Sherburne



A working model for norovirus infection of the intestine. Noroviruses bind specific carbohydrates on commensal bacteria (histo-blood group antigens

[HBGA] for human noroviruses) in the gut lumen; the virus:bacteria complex is transcytosed across intestinal epithelial cells (IEC); and the carbohydrate stimulates viral infection of underlying B cells. Credit: Stephanie M. Karst, Ph.D.

University of Florida researchers have grown a human norovirus in a cell culture dish, finally opening the door to developing medications for fighting the intestinal scourge that strikes tens of millions every year in schools, hotels and cruise ships worldwide.

"The biggest hurdle to doing norovirus research for its entire history—it was discovered in 1972—has been that we can't culture the human viruses in a cell culture dish," said UF Health researcher Stephanie Karst, an associate professor in the department of molecular genetics and microbiology in the UF College of Medicine. "That complicates every aspect of research. We can't study how it replicates, we can't test therapeutics and we can't generate live virus vaccines."

A paper authored by Karst and her colleagues appears Friday, Nov. 7, in the journal *Science*. Noroviruses are pernicious intestinal viruses. They cause violent vomiting and diarrhea, and people ill with the virus remain contagious up to three days after they seem to recover.

Although a vaccine for these viruses is in clinical trials, there is still no medication to combat them. That's in part because researchers have not been able to culture human noroviruses so they can test potential treatments—until now. According to the Centers for Disease Control and Prevention, in the United States, human noroviruses cause 19 million to 21 million cases of illness per year, and contribute to 56,000 to 71,000 hospitalizations and 570 to 800 deaths, mostly in young children and older adults. Noroviruses are resistant to many common

disinfectants. Very little of the virus is needed to infect a host, so a surface may still contain enough virus to infect a person even after it is cleaned.

Previously, researchers speculated that noroviruses primarily target intestinal epithelial cells, which line the intestine and protect it from pathogens, Karst said. However, this new research demonstrates that the virus targets B cells, a type of white blood cell common in the intestine.

"That's a big surprise," Karst said. "You would think that any virus that's going to target the intestine would instead target the intestinal epithelial cells because that's the first cell the virus is going to encounter."

Researchers also were surprised to find that bacteria present in the body's gut flora, also known as commensal bacteria, helped the human norovirus infect B cells. Karst said scientists have long known that noroviruses need a particular kind of carbohydrate to infect cells.

"What we've shown is that noroviruses attach to that carbohydrate expressed on commensal bacteria, and that this interaction stimulates viral infection of the B cell," Karst said. "This is a really exciting, emerging theme. A variety of intestinal viruses seem to exploit the bacteria that are present in our intestines all the time. These viral infections are enhanced by the presence of bacteria in the gut."

UF research scientist Melissa Jones, a co-author on the paper, said the idea to study B cells came from Karst's research on mouse noroviruses. UF scientists detected virus in Peyer's patches, pockets of lymphoid nodules that line the intestine and survey the organ for pathogens.

"Ultimately, this system should open up new avenues for norovirus vaccine and antiviral drug development," Karst said.

More information: "Enteric bacteria promote human and mouse norovirus infection of B cells". *Science* 7 November 2014: Vol. 346 no. 6210 pp. 755-759. DOI: 10.1126/science.1257147

Provided by University of Florida