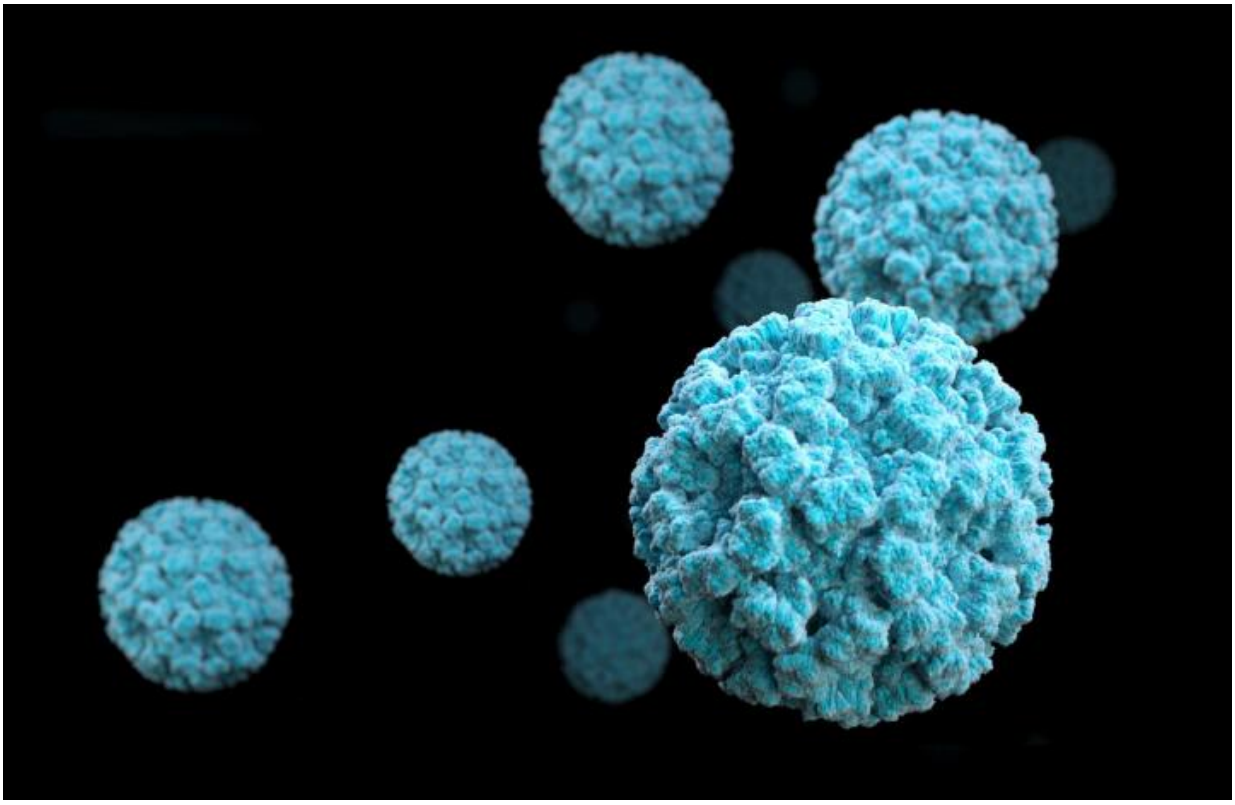
Molecules from breast milk and seaweed suggest strategies for controlling norovirus

July 26 2018



Norovirus. Credit: CDC

Norovirus is the most common cause of gastroenteritis worldwide; it causes tens hundreds of thousands of deaths each year and is particularly risky for children under 3 years old. If someone gets norovirus in a setting like a hospital, it's critically important to find a way to protect

others from getting infected. New research from several universities in Germany, to be published in the *Journal of Biological Chemistry*, suggests that it may be easier than anticipated to find a compound that could be used as a food supplement to stop the spread of norovirus in children's hospitals.

Norovirus causes disease after entering cells in the gut by binding to a sugar molecule called fucose, which is found on cell surfaces as part of the structure that determines human ABO blood types. Fucose is also found in breast milk and other foods. Norovirus can't tell the difference between fucoses that are part of cells in the gut and those that are simply passing through; for this reason, adding a fucose-based supplement to the diet as a decoy could be a way to capture the virus and keep it from infecting cells.

To develop this strategy, however, researchers needed to understand which features of fucose and virus molecules affected how well they attached to each other. In cells, foods, and milk, fucose is rarely found as a single molecule; rather, it's part of chains or networks of sugars and proteins. Franz-Georg Hanisch, a researcher at the University of Cologne, led a project to disentangle these molecular elements and understand what kind of fucose-based product would best distract noroviruses. He started by screening the many types of fucose-containing human milk oligosaccharides (HMOs).

To Hanisch's surprise, the strength of the binding between the norovirus protein and HMOs did not depend much on the specific structure of the HMO, or the types of fucose molecules it contained. Rather, what mattered was only how many fucoses it contained. Each individual fucose stuck weakly to the virus protein, but the more fucoses there were in the compound, the better the compound and the viral protein stuck together.

"The binding of the virus is not dependent in any way on further structural elements (of HMOs)," Hanisch said. "It's only the terminal fucose which is recognized, and the more fucose at higher densities is presented, the better is the binding."

Hanisch then turned to the industry standard of where to get a lot of fucose fast. Brown algae—the same family of seaweed that includes kelp—produce a compound called fucoidan, which is a complex network of many fucoses. (Fucoidan has independently been explored as a treatment for HIV, CMV, and HSV for unrelated biochemical reasons.)

"There are procedures for isolating the stuff in quite high yields and in high purity," Hanisch said.

The organization of the fucose in fucoidans looks nothing like any fucose-containing molecules found in the human body, but fucoidan nevertheless tightly bound to the virus protein in the team's experiments. This is good news, because it means that fucoidan could be a safe and cheap food additive to block viruses from infecting cells. It also suggests that the sky is the limit for researchers to design an even better fucose-containing compound.

Hanisch and his collaborators are therefore now moving on to experiments with live viruses and live organisms. The hope is to eventually have a fucose-based food supplement that could be given to a group of people, like hospitalized children, at the first sign of a norovirus outbreak, to prevent the circulating viruses from entering their cells and causing disease.

"I hope that in about three years we will have a product which can be used in norovirus defense and to go into clinical studies," Hanisch said.

More information: Franz-Georg Hanisch et al, Avidity of α-fucose on

human milk oligosaccharides and blood group-unrelated oligo/poly-fucoses is essential for potent norovirus binding targets, *Journal of Biological Chemistry* (2018). DOI: 10.1074/jbc.RA117.001369