'Mini-guts' offer clues to pediatric GI illness

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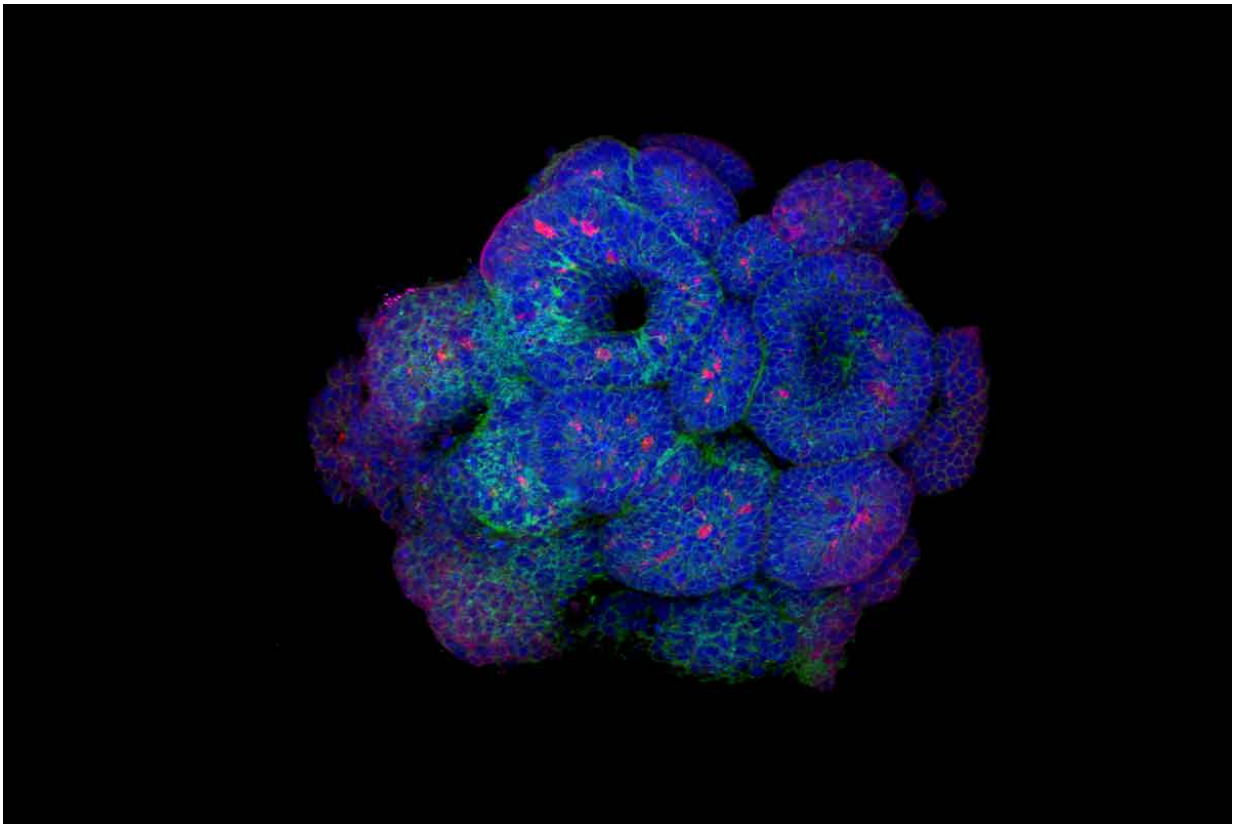


An image of an enteroid, a 'mini-gut' grown in a lab to study enteroviruses. The scientists isolated intestinal stem cells, grew them in culture and then stained them for various cell types. Credit: Cliff Luke/Misty Good

Using immature stem cells to create a miniature model of the gut in the laboratory, researchers at Washington University School of Medicine in St. Louis and the University of Pittsburgh have determined how

infection-causing enteroviruses enter the intestine.

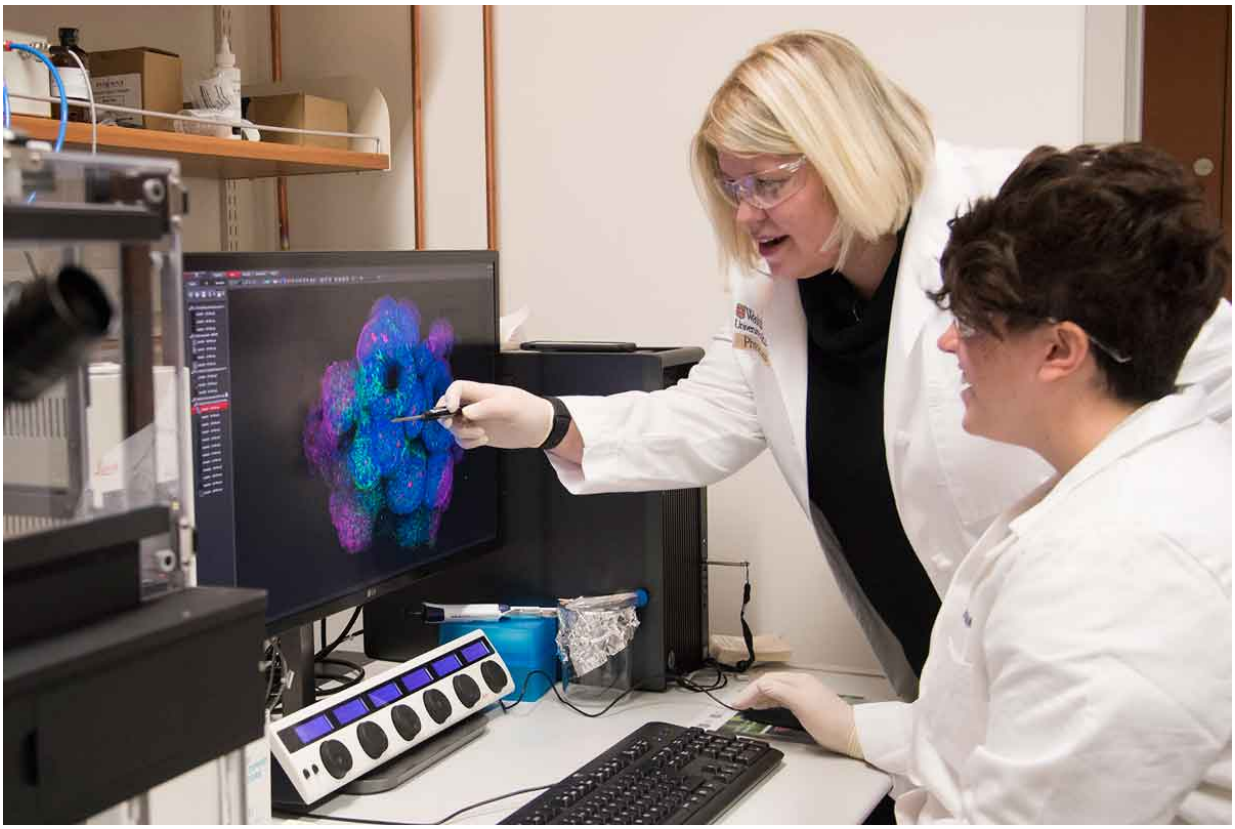
Enteroviruses cause millions of infections each year worldwide and are transmitted primarily through close person-to-person contact, touching infected surfaces, or ingesting food or water containing the virus. They can spur flu-like symptoms or more serious conditions such as inflammation in the brain or heart, acute paralysis or even death. Enterovirus infections within neonatal intensive care units (NICU) can be particularly devastating as infants are especially susceptible to infection from these viruses.

The study is published Jan. 30 in the online early edition of *Proceedings of the National Academy of Sciences*.

Within the pediatric population, enteroviruses have proved particularly devastating, with infant fatality rates approaching 20 percent.

"This study not only provides important insights into enterovirus infections but also provides an important model that could be used to test the efficacy of anti-enterovirus therapeutics in the premature intestine," said Misty Good, MD, an assistant professor of pediatrics at Washington University School of Medicine in St. Louis and co-senior author of the study.

Researchers isolated stem cells from a premature infant's small intestine and created "mini-guts" in the laboratory as a model to see how the virus behaves in the intestine. This model replicates various cell types within the tissue found in the intestine.



Washington University's Misty Good, MD, and research technician Alexa Bolock examine an image of an enteroid, a 'mini-gut' they and other researchers grew in the lab. Scientists at Washington University School of Medicine in St. Louis and the University of Pittsburgh used mini-guts to determine how infection-causing enteroviruses enter the intestine. Credit: Robert Boston

The mini-gut model showed that the small intestines are most susceptible to infection by certain enteroviruses such as echovirus 11 (E11) and coxsackievirus B (CVB), both of which are commonly associated with illness in the neonatal population. E11, the enterovirus most commonly associated with NICU infections, induced significant damage to the mini-guts.

Researchers also found that E11 targets certain cells within the

gastrointestinal tract and may facilitate passage of the virus into the bloodstream, which can result in serious illness.

"Despite their major global impact, especially on the health of children, little is known about the route that these viruses take to cross the intestine, their primary point of entry," said co-senior author Carolyn Coyne, PhD, an associate professor of microbiology and molecular genetics at the University of Pittsburgh School of Medicine. "Our approach has for the first time shed some light on this process. This model also could be used for developing anti-enterovirus therapeutics targeting the gastrointestinal tract, given that no therapeutic approaches exist to combat infections of these viruses."

Said Gary A. Silverman, MD, PhD, the Harriet B. Spoehrer Professor and the head of Department of Pediatrics at Washington University: "This research has the potential for a positive global impact on human health, especially since enteroviruses cause disease in all human populations and age groups."

More information: Enteroviruses infect human enteroids and induce antiviral signaling in a cell lineage-specific manner, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1617363114

Provided by Washington University School of Medicine