Researchers engineer functioning small intestine in laboratory experiments

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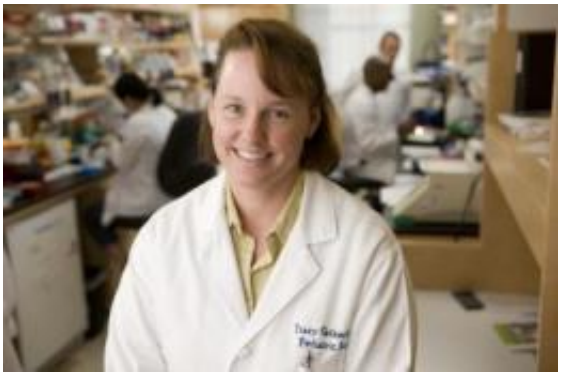

Tracy C. Grikscheit, MD works at the Saban Research Institute of Children's Hospital Los Angeles. Credit: Photo courtesy of Children's Hospital Los Angeles

Researchers at The Saban Research Institute of Children's Hospital Los Angeles have successfully created a tissue-engineered small intestine in mice that replicates the intestinal structures of natural intestine -- a necessary first step toward someday applying this regenerative medicine technique to humans.

The study led by Tracy C. Grikscheit, MD —"A Multicellular Approach Forms a Significant Amount of Tissue-Engineered Small Intestine in the Mouse"— has been published in the July issue of *Tissue Engineering Part A,* a premier biomedical journal.

"In this paper, we are able to report that we can grow tissue-engineered

intestine in a mouse model, which opens the doors of basic biology to understand how to grow this tissue better," said Dr. Grikscheit, who is also an assistant professor of surgery at the Keck School of Medicine of the University of Southern California.

As a pediatric surgeon, Dr. Grikscheit is concerned with finding solutions for some of her more vulnerable patients—newborns. Infants born prematurely are at increased risk for a gastrointestinal disease called necrotizing enterocolitis (NEC), which occurs when the intestine is injured. The cause is unknown.

Early treatment of NEC is essential to stop the potentially life-threatening leakage of bacteria into the abdomen. Often, the only solution is surgical removal of the small intestine. However, this option leaves the baby dependent on intravenous feeding and at risk for liver damage from subsequent intravenous nutrition. Organ transplants are possible but not a long-term solution, with only a 50 percent chance the grafted intestine will last past the child's 5th birthday.

Dr. Grikscheit, a member of The Saban Research Institute's Developmental Biology and Regenerative Medicine program, envisions a better solution. "The small intestine is an exquisitely regenerative organ. The cells are constantly being lost and replaced over the course of our entire lives," she explained. "Why not harness that regenerative capacity to benefit these children?"

Working in the laboratory, the research team took samples of intestinal tissue from mice. This tissue was comprised of the layers of the various cells that make up the intestine — including muscle cells and the cells that line the inside, known as epithelial cells. The investigators then transplanted that mixture of cells within the abdomen on biodegradable polymers or "scaffolding."

What the team wanted to happen did — new, engineered small intestines grew and had all of the cell types found in native intestine. Because the transplanted cells had carried a green label, the scientists could identify which cells had been provided — and all of the major components of the tissue-engineered intestine derived from the implanted cells. Critically, the new organs contained the most essential components of the originals.

"What is novel about this research is that this tissue-engineered intestine contains every important cell type needed for functional intestine. For children with intestinal failure, we are always looking for long-term, durable solutions that will not require the administration of toxic drugs to ensure engraftment. This tissue-engineered intestine, which has all of the critical components of the mature intestine, represents a truly exciting albeit preliminary step in the right direction," said Henri Ford, MD, Vice President and Surgeon-in-Chief at Children's Hospital Los Angeles.

"We demonstrated that we are providing all of the important cells—the muscle, nerve, epithelium, and some of the blood vessels," noted Frédéric Sala, PhD, lead author. "All of these are critical to proper functioning of the tissue, and now we know their origins." Next up are additional tissue-growing experiments—each one of which may bring that much closer the prospects of clinical testing and a solution for babies in need.

Provided by Children's Hospital Los Angeles