

# GUTSY WONDER

A future strategy for  
tissue-engineered intestine

Infants born prematurely are at increased risk for many problems, including a gastrointestinal disease called necrotizing enterocolitis, known as NEC. Since NEC is often associated with a rapid clinical deterioration that can result in death, early treatment is essential.

Sometimes, in spite of every medical intervention, treatment fails, and a difficult decision must be made to stop bacteria from leaking into the abdomen from the severely damaged intestine, causing a life-threatening infection. As the surgeon removes the diseased small intestine, the child's life has been forever changed.

Without an adequate length of small intestine, the child cannot digest food or absorb nutrients. The baby's survival will depend upon total parenteral nutrition (TPN), a form of intravenous feeding. Further complicating this already cloudy picture is the risk associated with long-term use of TPN—liver damage is common, especially in pre-term infants.

Another option for this baby is a small intestine transplant. However, there is only a 50 percent chance that the grafted organ will last as long as five years, and the child will require many medications for immunosuppression to "tolerate" the transplanted organ.

Is that really the best that modern medicine can do for these very small patients? Tracy Grikscheit, MD, doesn't think so. Grikscheit is an investigator at The Saban Research Institute of Children's Hospital Los Angeles and an assistant professor of Surgery at the Keck School of Medicine of the University of Southern California.

"I believe the solution for these problems will come from within," she says. "The small intestine is an exquisitely regenerative organ. The cells are constantly being lost and replaced over the course of our entire lives. Why not harness that regenerative capacity to benefit these children?"

After an initial "proof of concept" study in rats, Grikscheit performed an experiment in 6-week-old pigs since they are similar in size to premature newborns. Results of this study appeared in the *Journal of Surgical Research*. First, Grikscheit used a biodegradable scaffolding

and "seeded" it with stem cells harvested from the intestinal walls of adult pigs. She then placed the structure into the baby pig's abdomen, in a place with a sufficient blood supply, and closed the incision.

The small intestine is composed of a number of different cell types: epithelium, muscle, nerve and blood vessels. Grikscheit wondered two things: would the implanted stem cells be able to differentiate into the various cell types, and would the cells grow in the appropriate places so that the engineered structure could actually function as a small intestine?

Seven weeks later, she removed the engineered intestine and examined it under a microscope. It looked like a small intestine. The cells had aligned themselves into perfect formation. They "knew" what to do. Not only had the cells formed the microscopic structures present in the small intestine, but they also had developed an adequate blood and nerve supply.

Anatomically, the engineered small intestine has everything it needs to work. In preliminary experiments, Grikscheit has implanted the tissue-engineered small intestine into pigs, and it appears to contain all of the relevant components of functioning intestine. If careful follow-up studies confirm these early results, clinical testing is not far off.

Just a short length of engineered intestine could change the future for those very small patients who now face an uncertain outlook. Grikscheit sums it up: "Many patients won't need tissue-engineered intestine. But for those patients who do, it could change their lives."



"I believe the solution for these problems will come from within ... Why not harness that regenerative capacity to benefit these children?"

Tracy Grikscheit, MD

