Researchers grow functional tissue-engineered intestine from human cells

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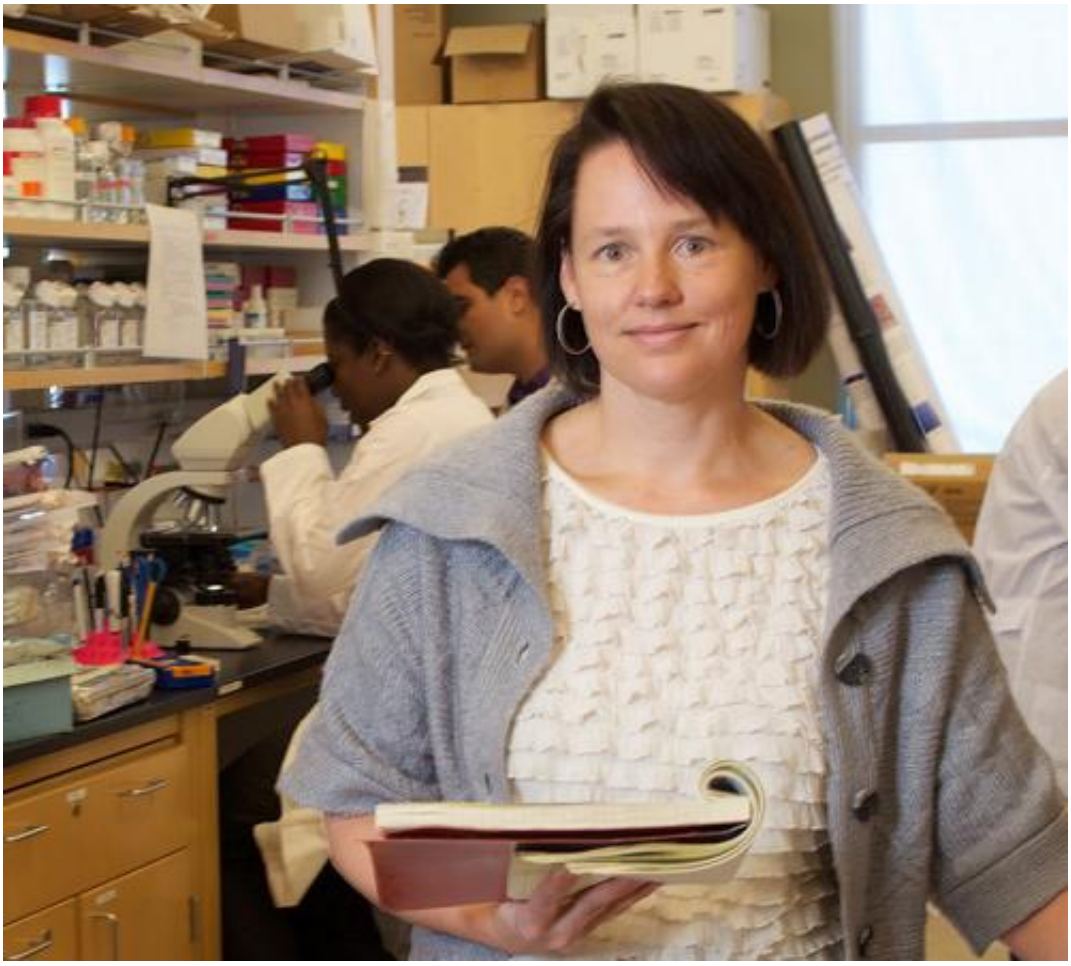

Tracy C. Grikscheit of The Saban Research Institute of Children's Hospital Los Angeles. Credit: Children's Hospital Los Angeles

A new study by researchers at Children's Hospital Los Angeles has

shown that tissue-engineered small intestine grown from human cells replicates key aspects of a functioning human intestine. The tissue-engineered small intestine they developed contains important elements of the mucosal lining and support structures, including the ability to absorb sugars, and even tiny or ultra-structural components like cellular connections.

Published online January 8 by the *American Journal of Physiology: GI & Liver*, the work brings surgeons one step closer to helping human patients using this regenerative medicine technique.

Tissue-engineered small intestine (TESI) grows from stem cells contained in the intestine and offers a promising treatment for short bowel syndrome (SBS), a major cause of intestinal failure, particularly in premature babies and newborns with congenital intestinal anomalies. TESI may one day offer a therapeutic alternative to the current standard treatment, which is intestinal transplantation, and could potentially solve its largest challenges - donor shortage and the need for lifelong immunosuppression.

Tracy C. Grikscheit, MD, a principal investigator in The Saban Research Institute of CHLA and its Developmental Biology and Regenerative Medicine program, is also a pediatric surgeon at Children's Hospital Los Angeles and an assistant professor of surgery at the Keck School of Medicine of the University of Southern California.

Grikscheit aims to help her most vulnerable young patients, including babies who are born prematurely and develop a devastating disease called necrotizing enterocolitis (NEC), where life-threatening intestinal damage requires removal of large portions of the small intestine. Without enough intestinal length, the babies are dependent on intravenous feeding, which is costly and may cause liver damage. NEC and other contributors to intestinal failure occur in 24.5 out of 100,000

live births, and the incidence of SBS is increasing. Nearly a third of patients die within five years.

CHLA scientists had previously shown that TESI could be generated from human small intestine donor tissue implanted into immunocompromised mice. However, in those initial studies - published in July 2011 in the biomedical journal Tissue Engineering, Part A - only basic components of the intestine were identified. For clinical relevance, it remained necessary to more fully investigate intact components of function such as the ability to form a healthy barrier while still absorbing nutrition or specific mechanisms of electrolyte exchange.

The new study determined that mouse TESI is highly similar to the TESI derived from human cells, and that both contain important building blocks such as the stem and progenitor cells that will continue to regenerate the intestine as a living tissue replacement. And these cells are found within the engineered tissue in specific locations and in close proximity to other specialized cells that are known to be necessary in healthy human intestine for a fully functioning organ.

"We have shown that we can grow tissue-engineered small intestine that is more complex than other stem cell or progenitor cell models that are currently used to study intestinal regeneration and disease, and proven it to be fully functional as it develops from human cells," said Grikscheit. "Demonstrating the functional capacity of this tissue-engineered intestine is a necessary milestone on our path toward one day helping patients with intestinal failure."

Provided by Children's Hospital Los Angeles

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