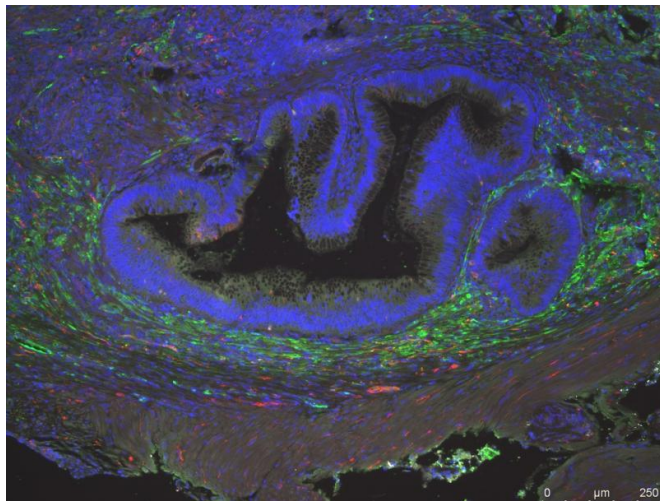


# Tissue-engineered colon from human cells develop different types of neurons

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Tissue-engineered colon generated from cells from a patient with Hirschsprung's disease. Nerve cells (derived from neurospheres) are shown in green. Credit: Children's Hospital Los Angeles

A study by scientists at Children's Hospital Los Angeles has shown that tissue-engineered colon derived from human cells is able to develop the many specialized nerves required for function, mimicking the neuronal population found in native colon. These specialized neurons, localized in the gut, form the enteric nervous system, which regulates digestive tract motility, secretion, absorption and gastrointestinal blood flow. In addition, in a condition called Hirschsprung's disease or aganglionosis, where those neurons are not present, the team was able to replace them.

The study—the first report on the enteric [nervous system](#) in human-derived tissue-engineered colon—was published online ahead of print in the journal of *Tissue Engineering, Part A* on September 28.

In healthy intestines, food is moved along the

[digestive tract](#) through peristalsis—a series of wave-like contractions. Special [nerve cells](#) called [ganglion cells](#) are required for this movement, but there is also a rich mixture of other types of nerve cells. In children with Hirschsprung's disease, these cells are missing. Without them, the intestine becomes blocked and surgical removal of the affected segment of colon is required.

To help these and other children suffering from intestinal diseases that may require surgical removal of all or part of their intestine, the CHLA team—led by principal investigator Tracy C. Grikscheit, MD, a pediatric surgeon and researcher at The Saban Research Institute of CHLA—is developing tissue-engineered options for these children.

One objective of growing tissue-engineered organs is to generate new tissue from a patient's own cells. Grikscheit and her team first needed to determine what parts of the enteric nervous system were present in tissue-engineered colon when it is grown from normal [human cells](#).

"The diversity of neuron types that grew within the human tissue-engineered colon was a revelation to our team, because previously we had only documented that some ganglia were present," said Grikscheit, who is also a tenured associate professor of Surgery at the Keck School of Medicine of the University of Southern California. "The next step was to determine if these neuronal elements could be supplied to tissue-engineered colon that was missing neurons - like in Hirschsprung's disease."

The scientists initially grew cells from patients with Hirschsprung's disease and from mice with a genetic mutation that causes aganglionosis. In both cases, the tissue-engineered colon derived from these cells did not have the all-important components of the intestinal nervous system. In a second set of experiments, again testing both

mouse and human cells, the investigators added neurospheres, which are clusters of purified [neural progenitor cells](#). The cells had been stained with green fluorescence, so the scientists could readily visualize where the nerve cells ended up in the tissue-engineered colon, as well as determine the source of the nerve cells.

"After growing the colon for four weeks, we saw that the green nerve [cells](#) had been incorporated into the colon engineered from human tissue derived from a patient lacking those elements and that the different nerve subtypes were present," said first author on the study, Minna Wieck, MD, an investigator and surgical resident at CHLA.

**More information:** *Tissue Engineering, Part A* ,  
[online.liebertpub.com/doi/pdf/...  
89/ten.TEA.2015.0120](https://online.liebertpub.com/doi/pdf/.../89/ten.TEA.2015.0120)

Provided by Children's Hospital Los Angeles

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